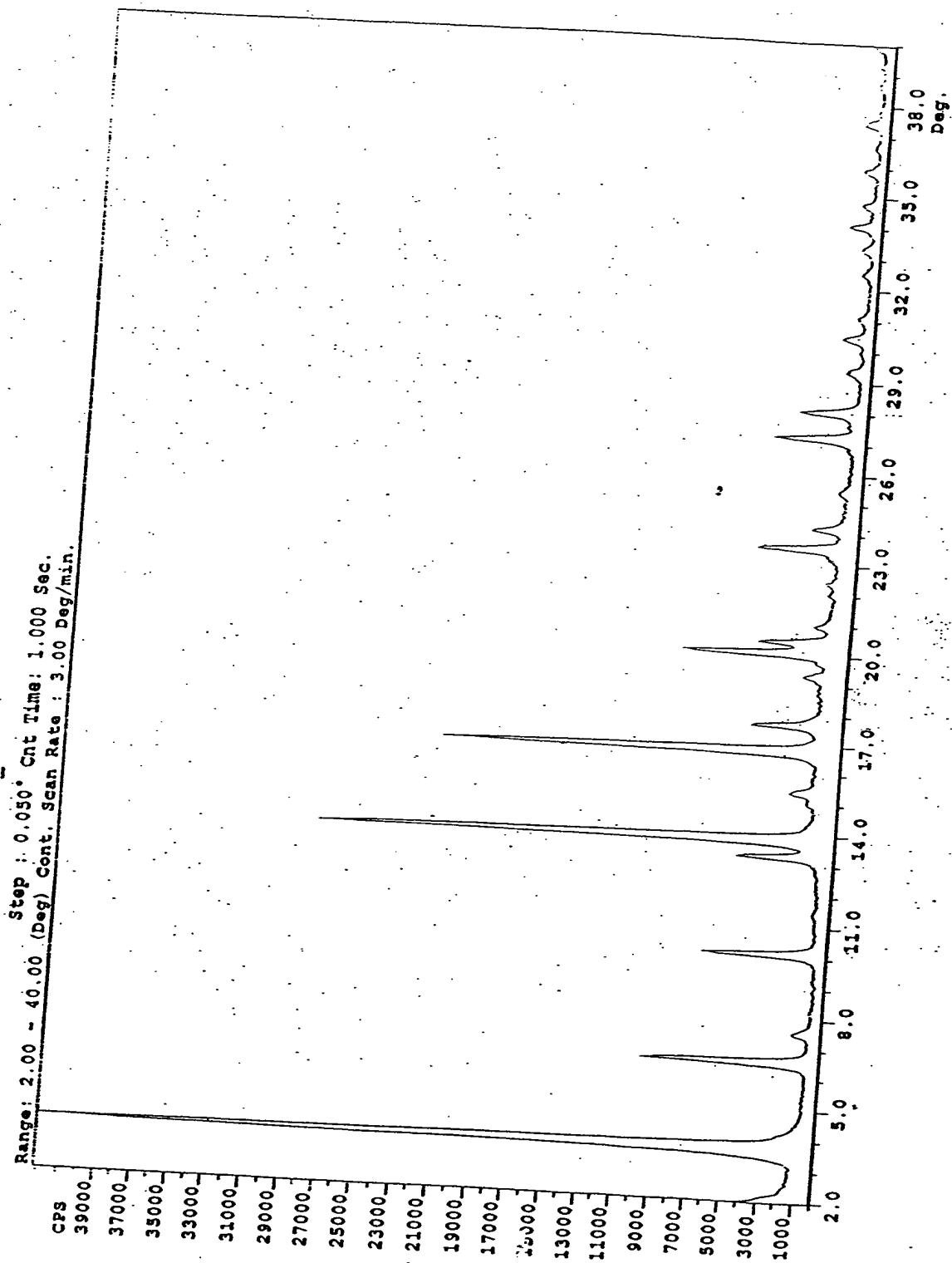


Fig 1

A



BEST AVAILABLE COPY

FIG. 2 C

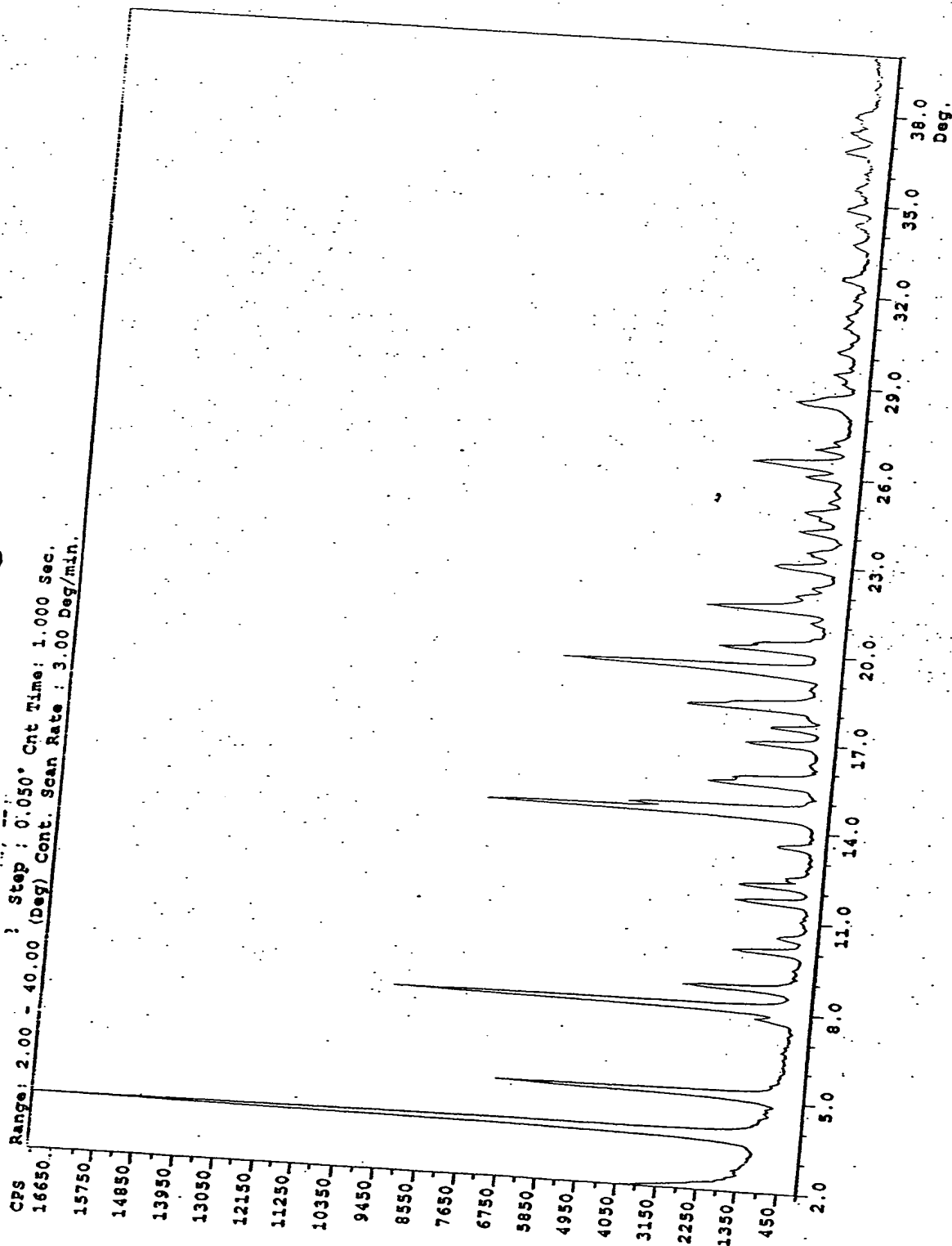


Fig 3 D

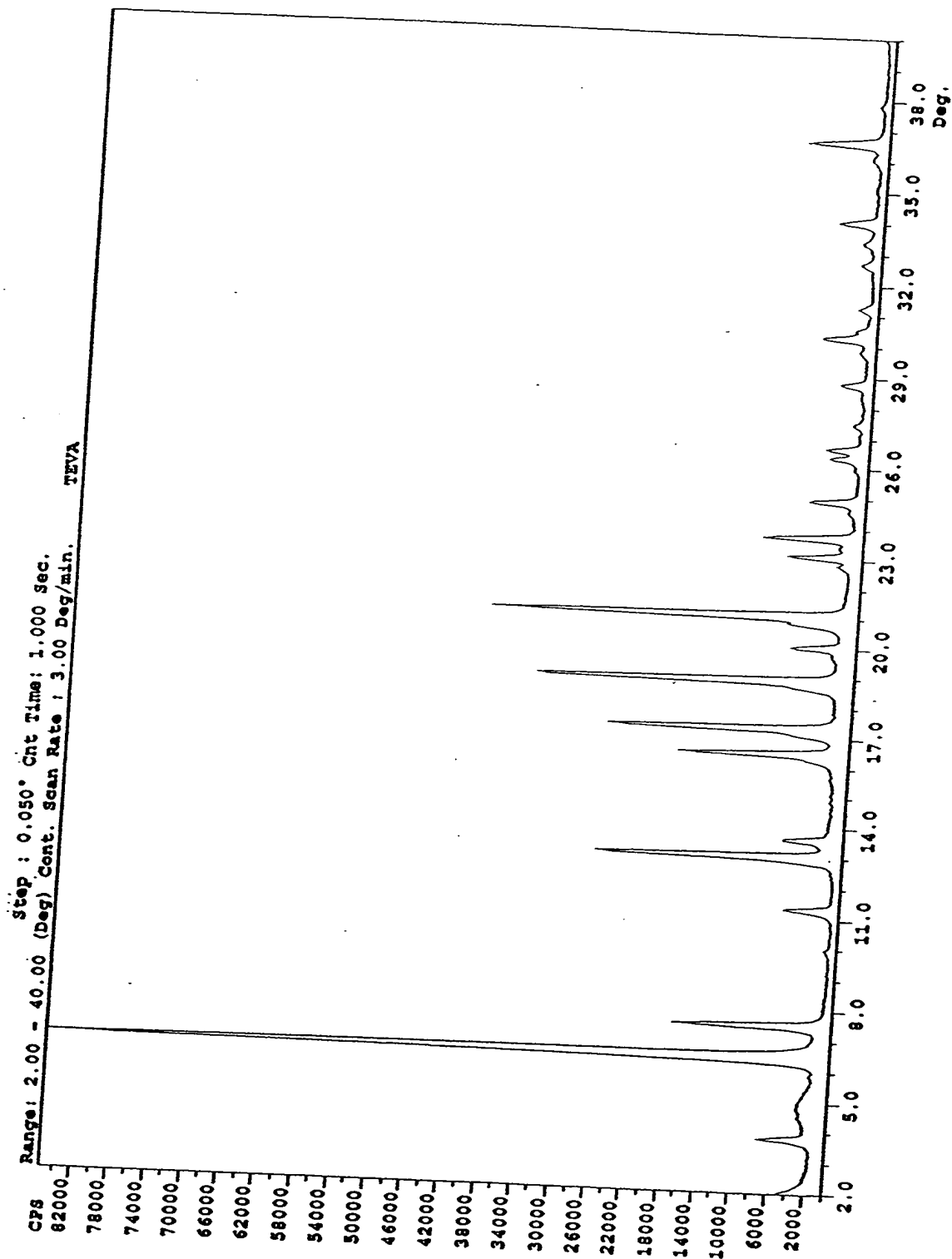


Fig 4 .E

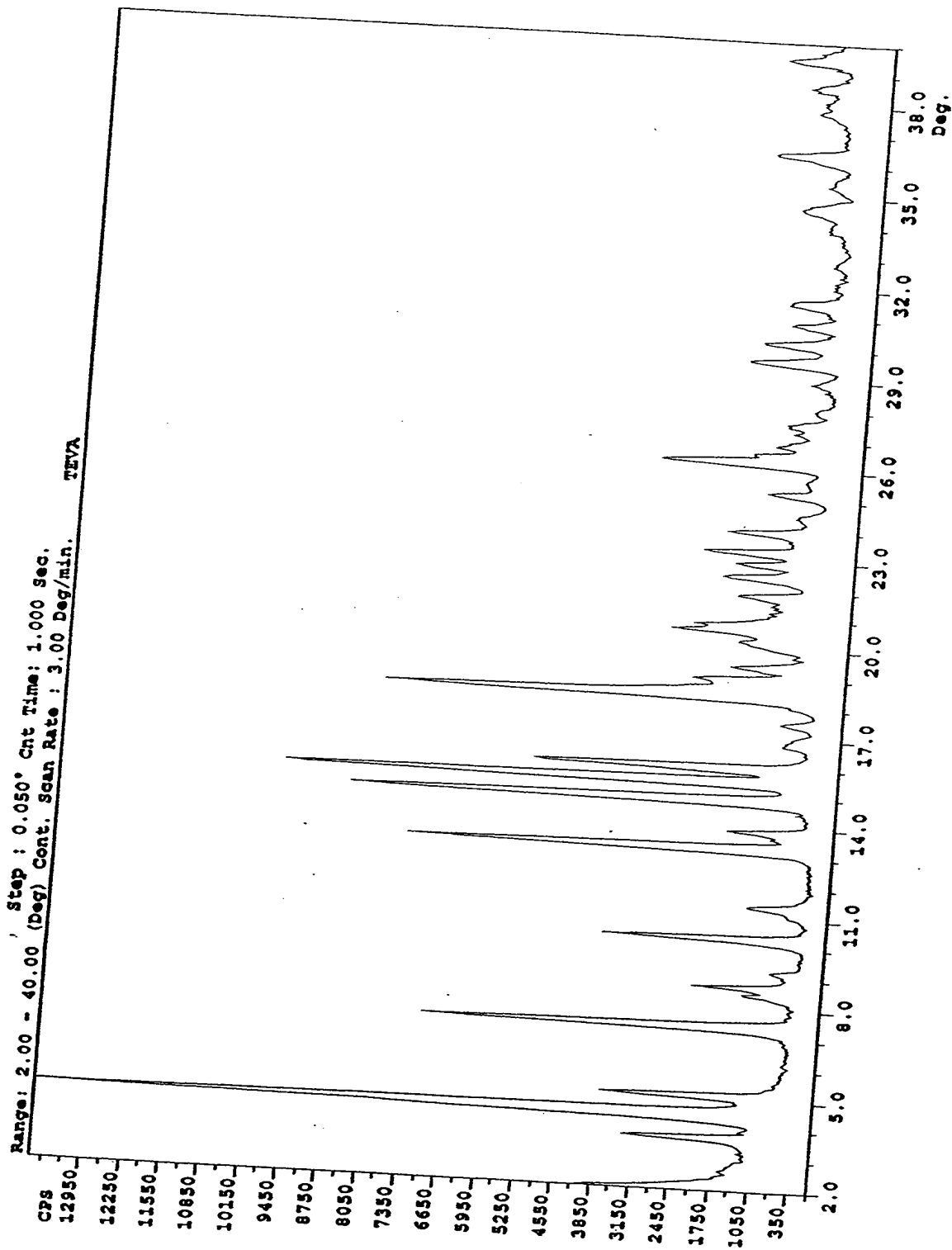


Fig. 5

F

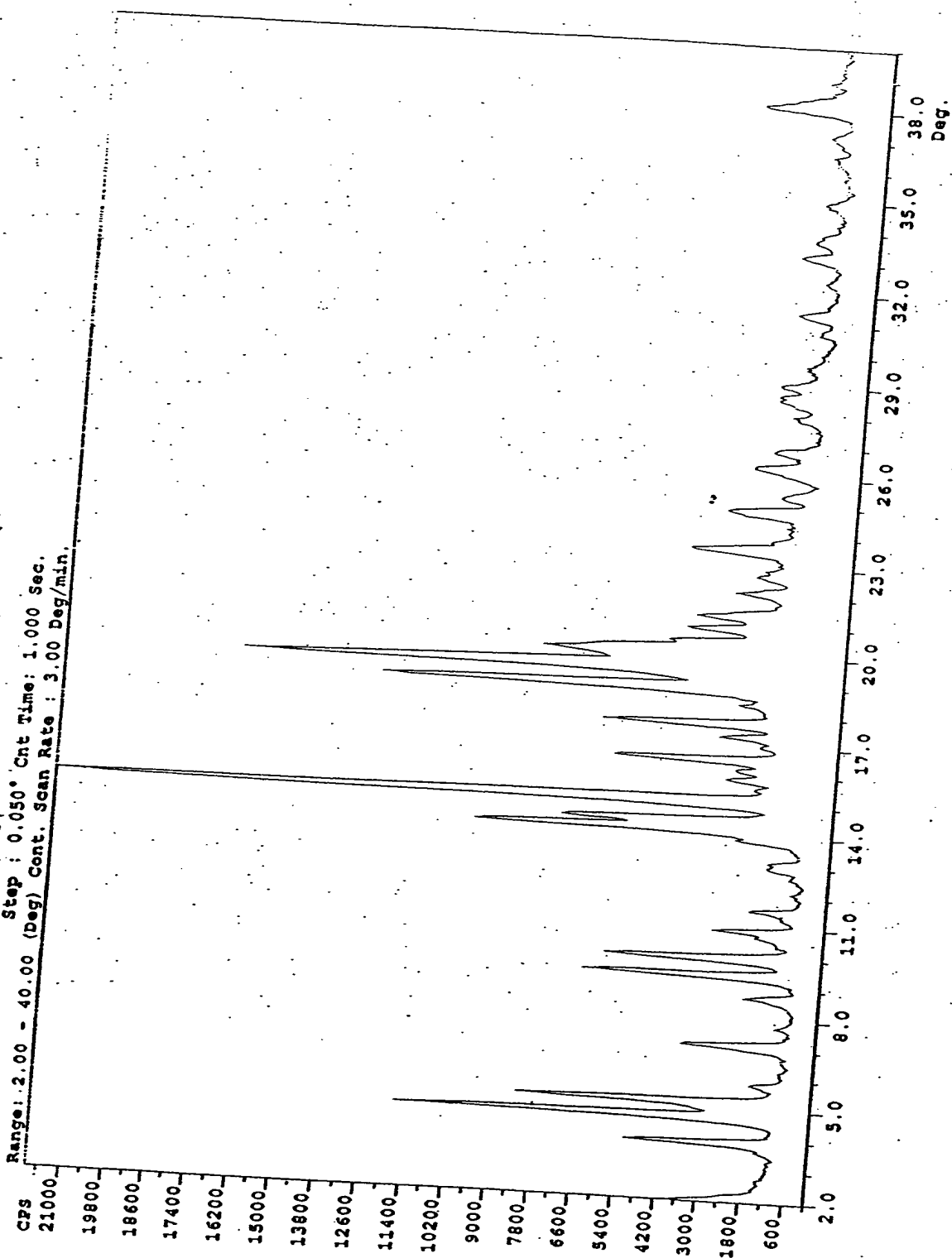


Fig. 6

G

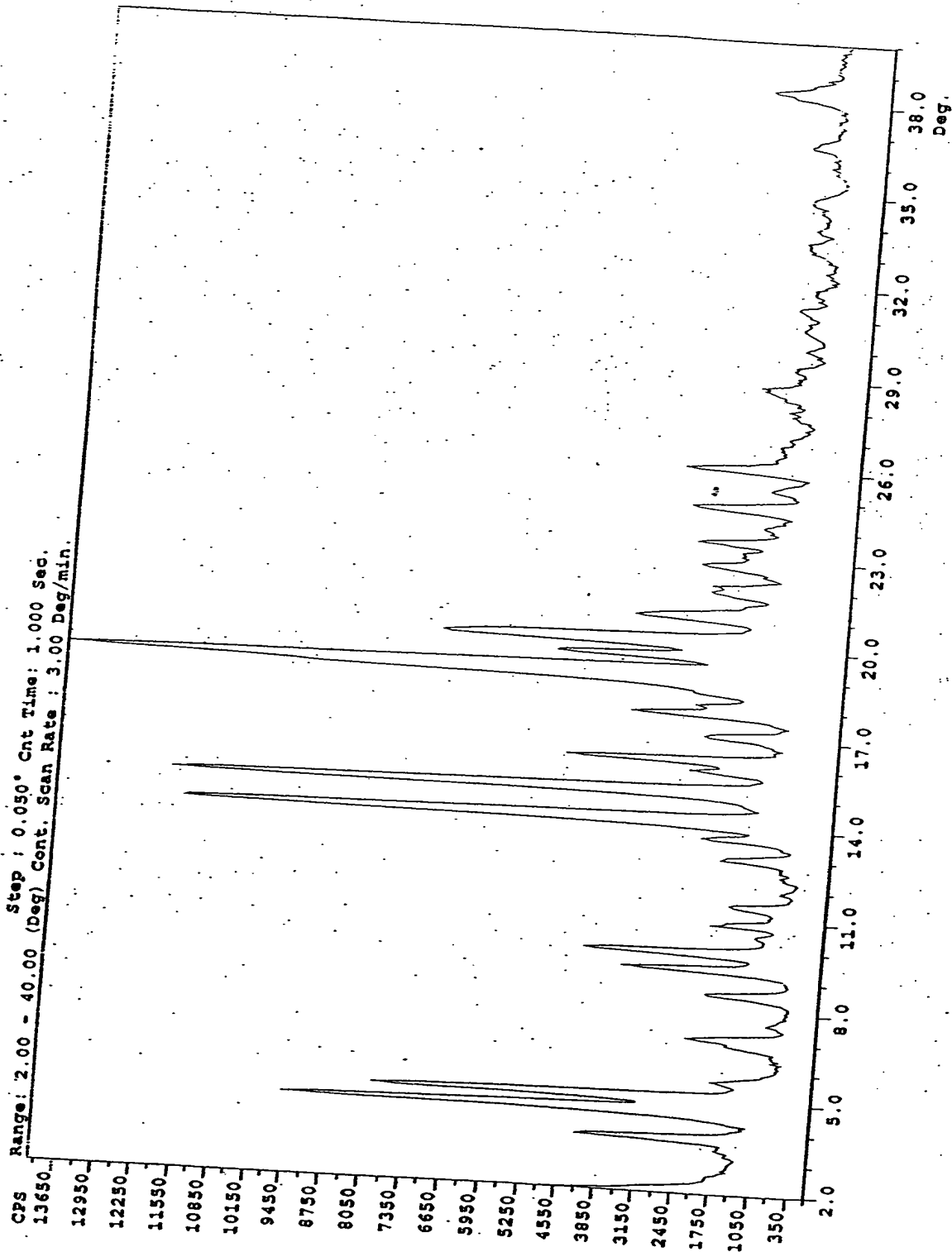


Fig 7 I

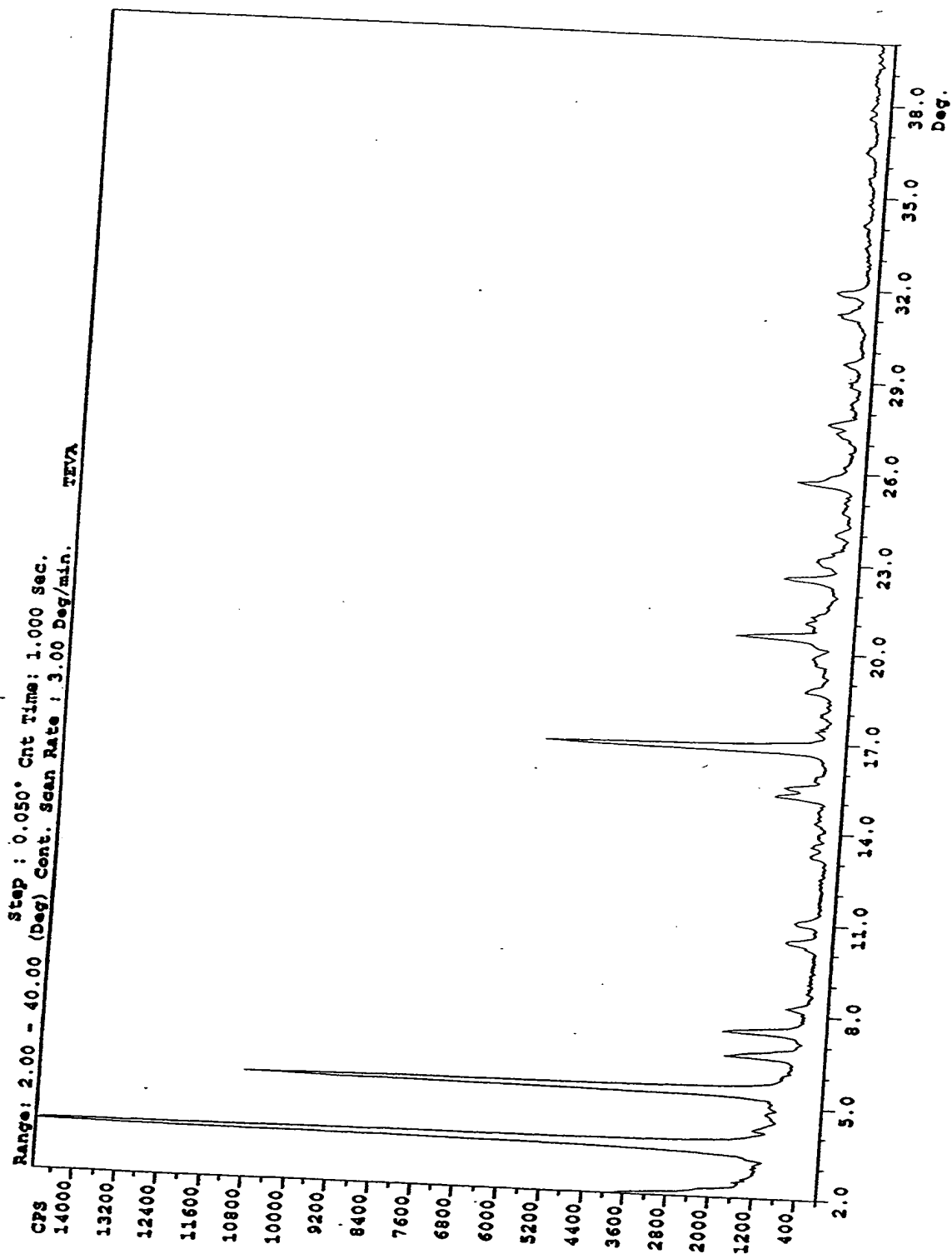


Fig. 8 3

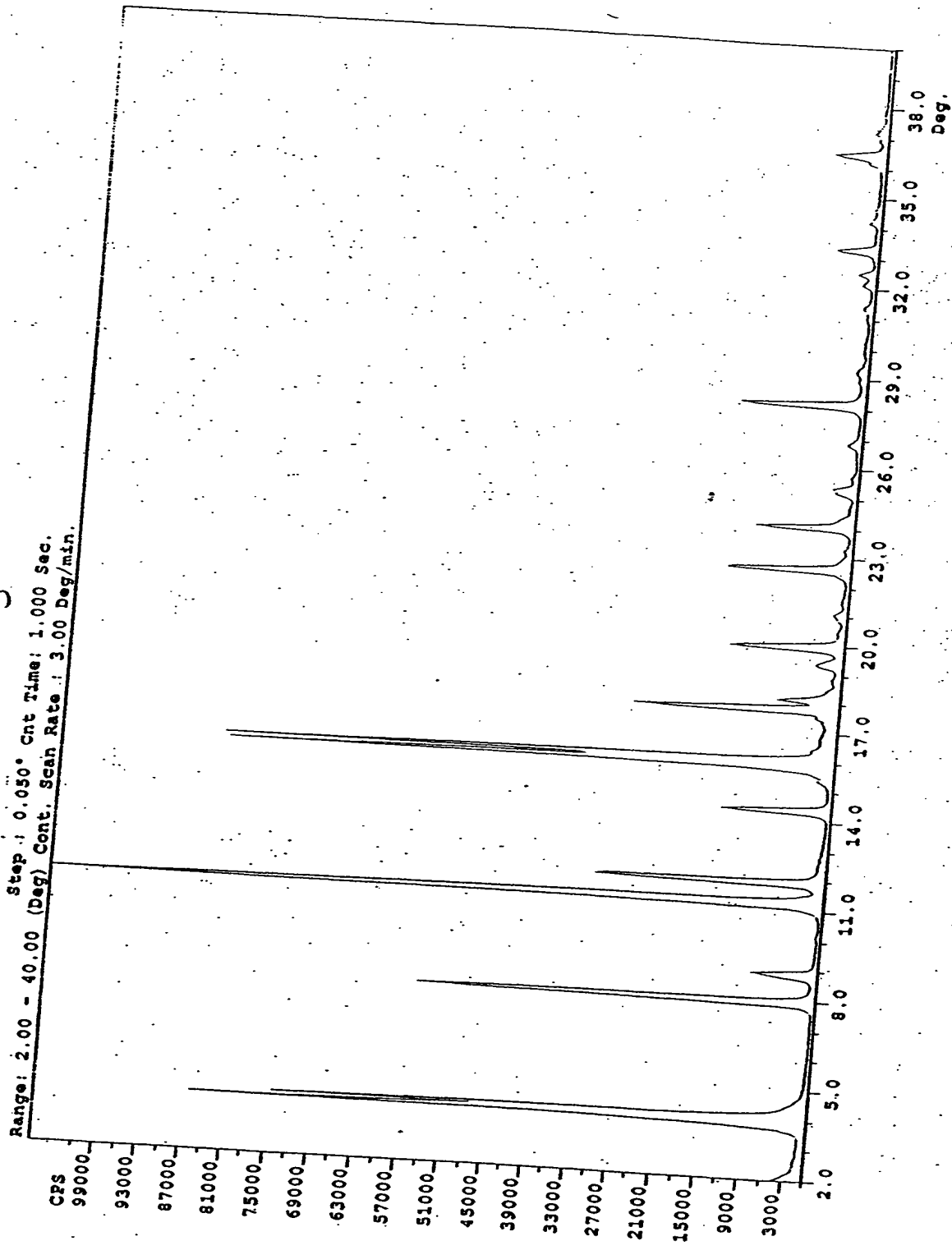




Fig. 9

K

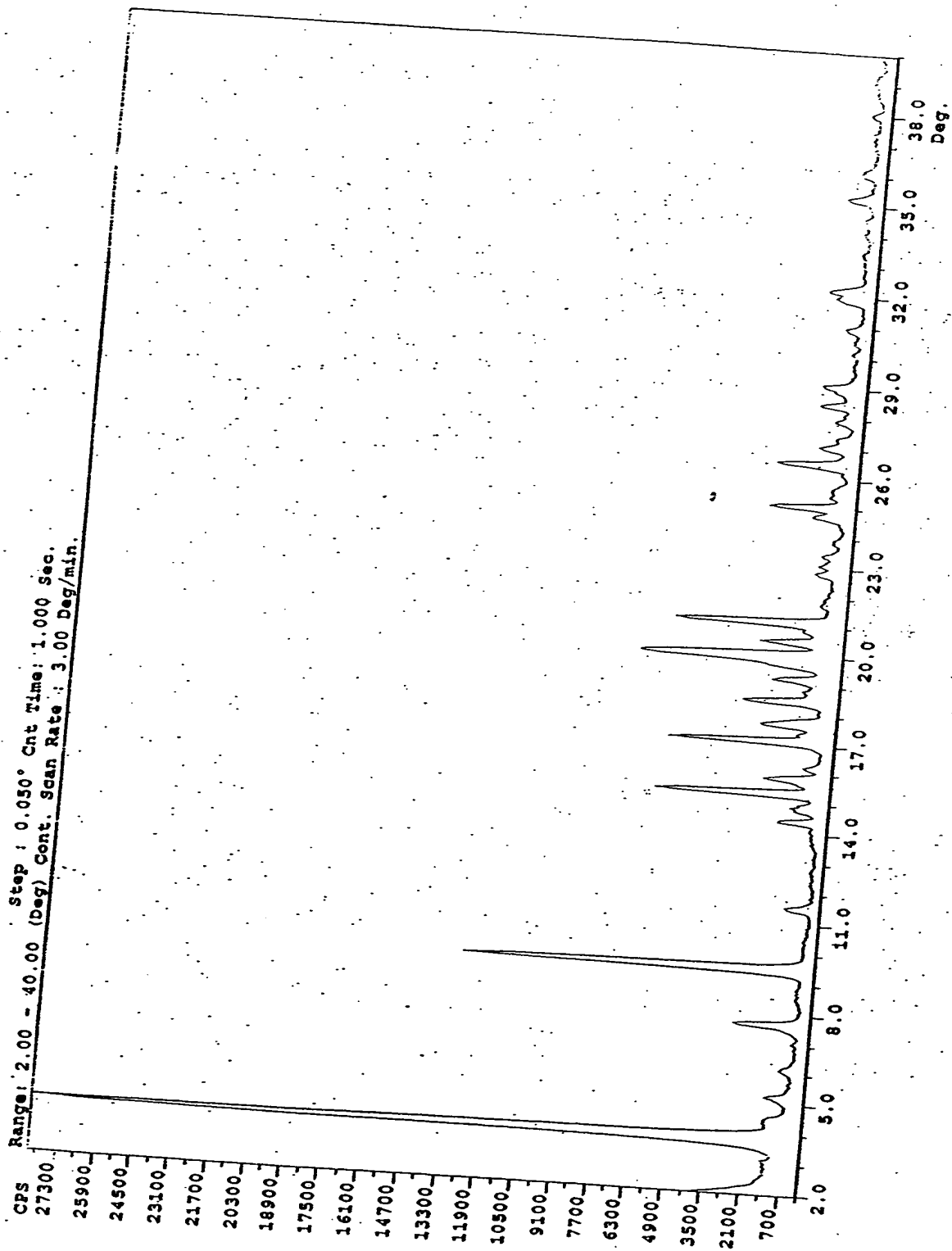


Fig. 10 L

Range: 2.00 - 40.00 (Deg) Cnt Time: 1.000 Sec.  
Step: 0.050 (Deg) Cont. Scan Rate: 3.00 Deg/min.

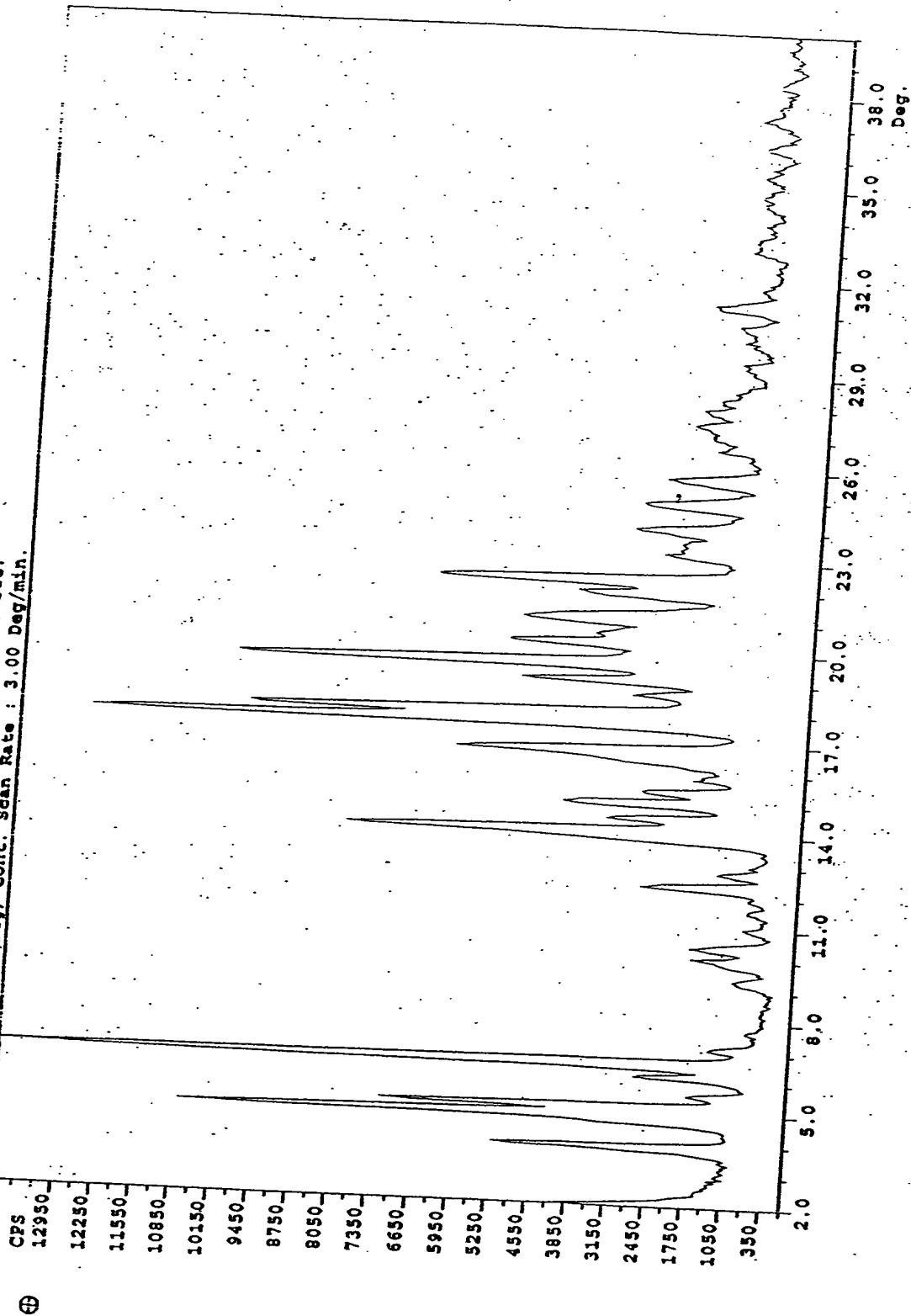


Fig. 11

M

Range: 2.00 - 40.00 (Deg) Cnt Time: 1.000 Sec.  
Step: 0.050 (Deg) Cont. Scan Rate: 3.00 Deg/min.

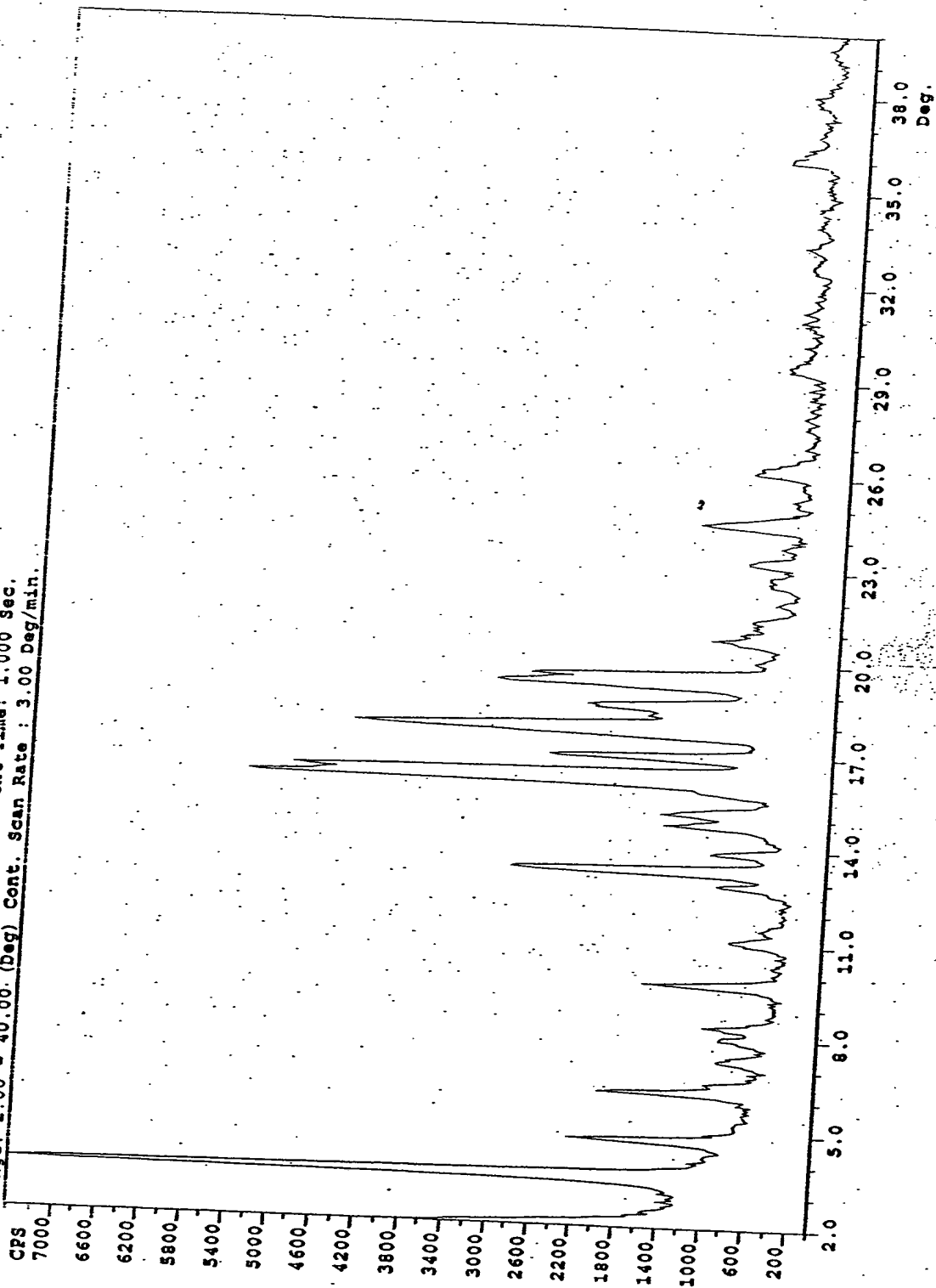


Fig. 12 N

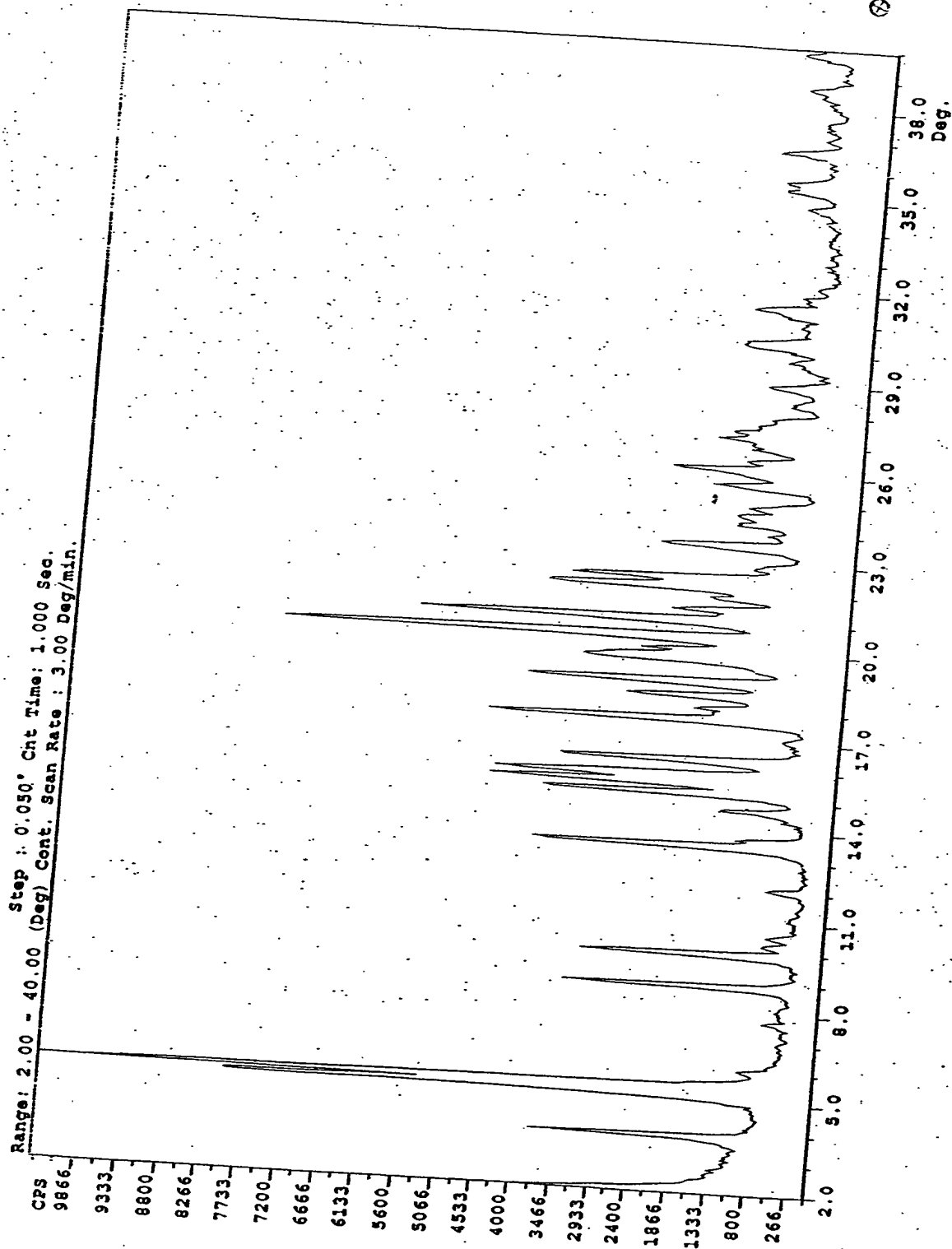


Fig. 13 0

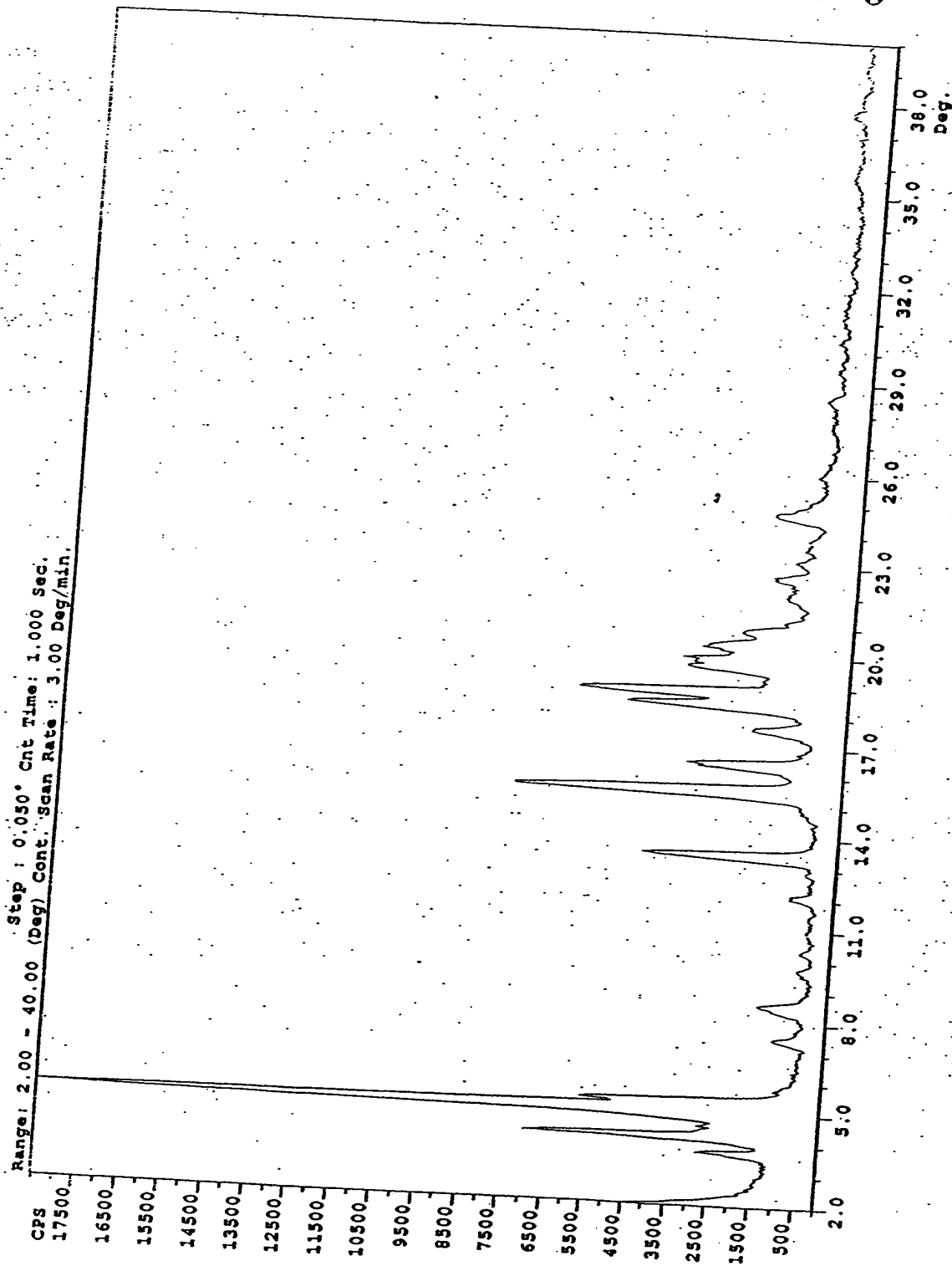


Fig. 14

P

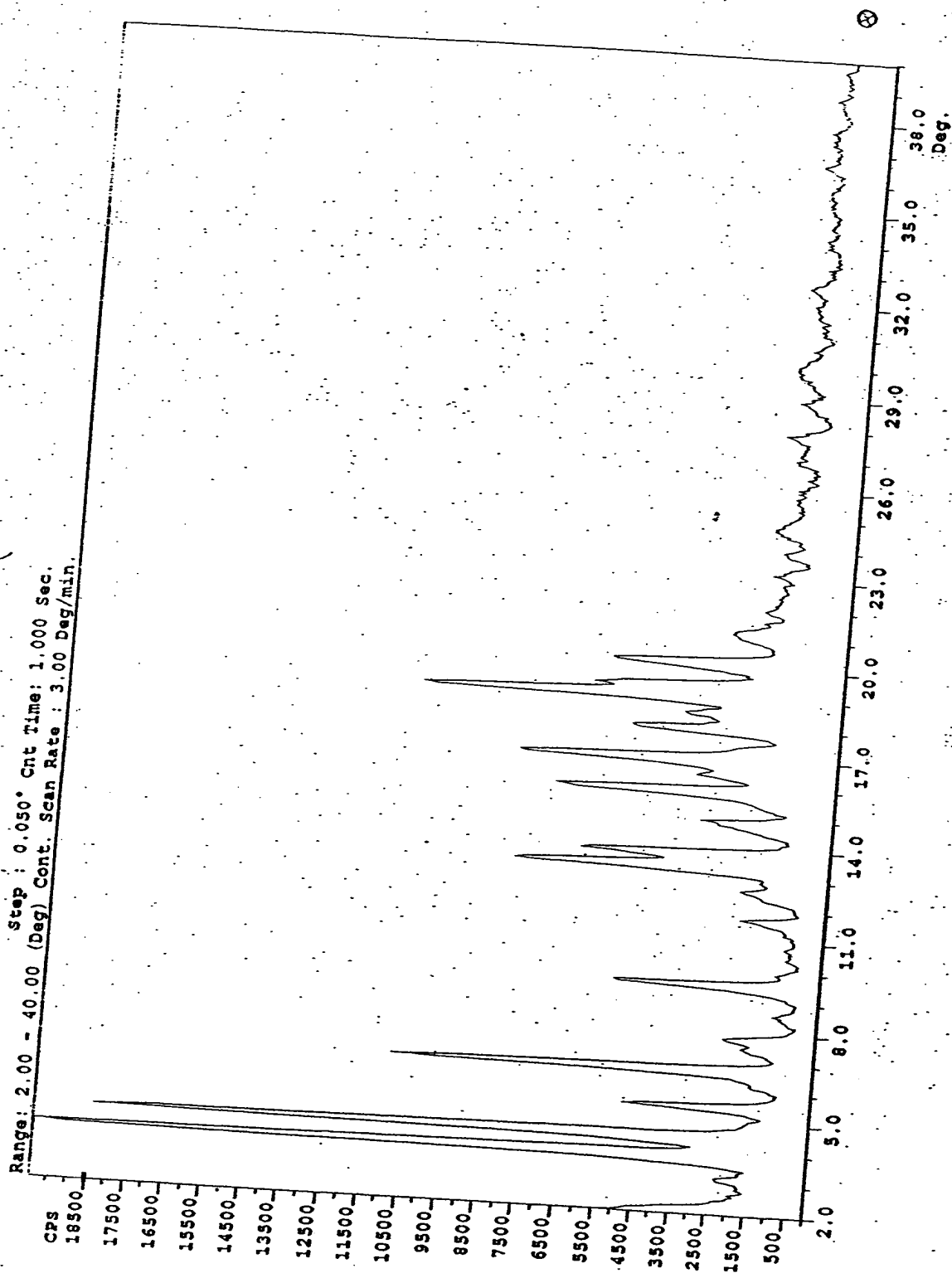


Fig. 15 Q

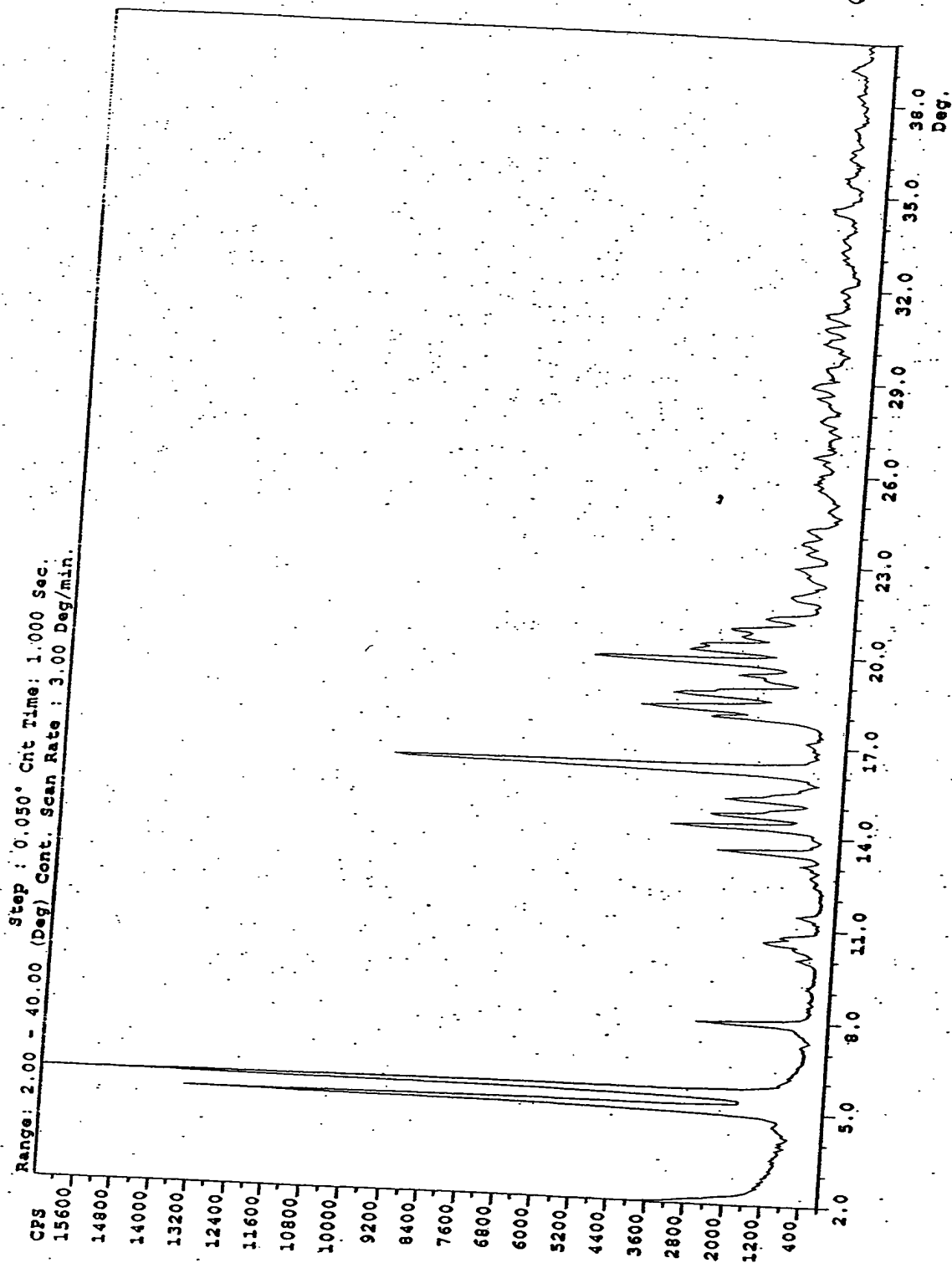


Fig. 16

T

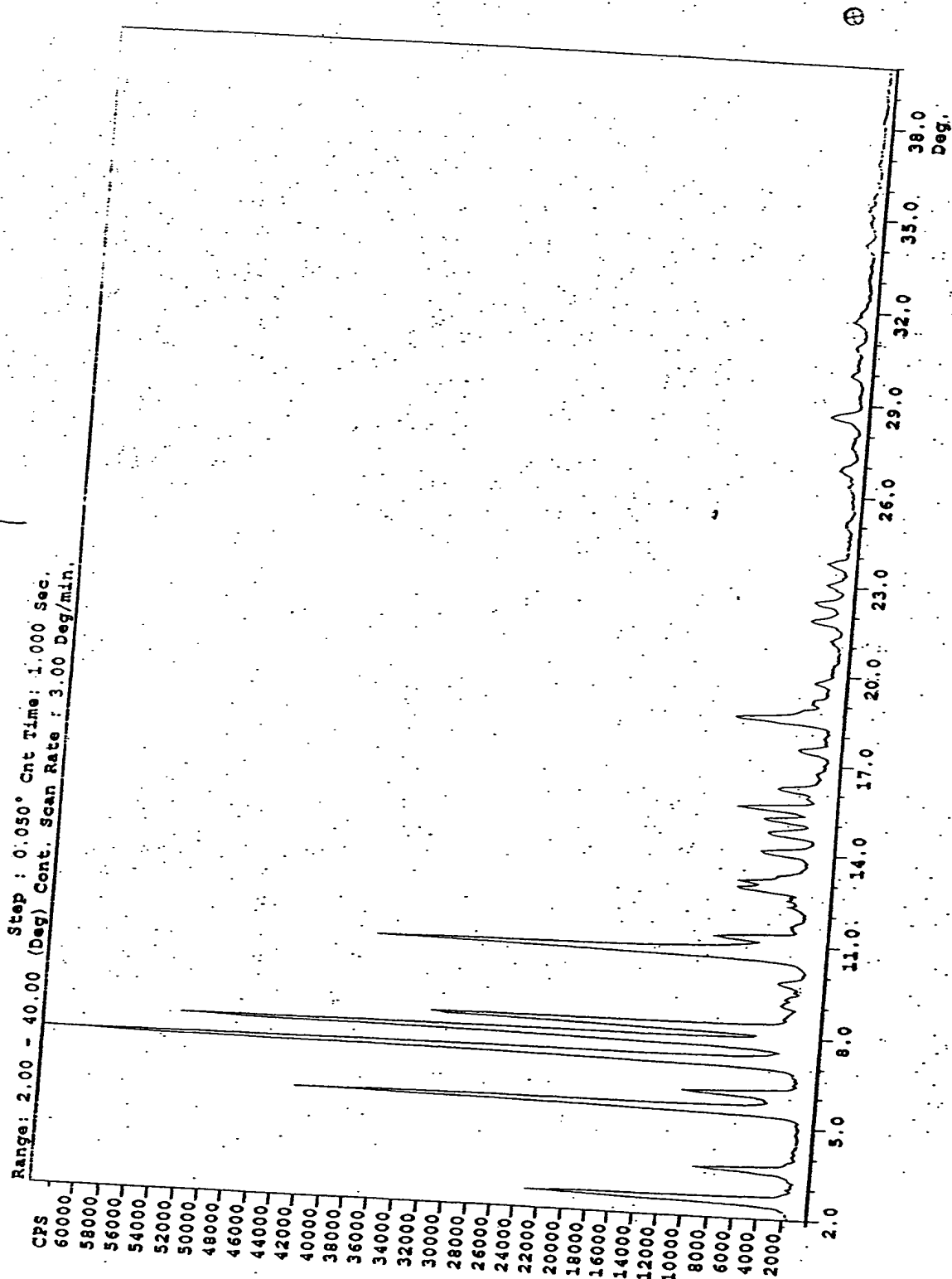




Fig. 17 u

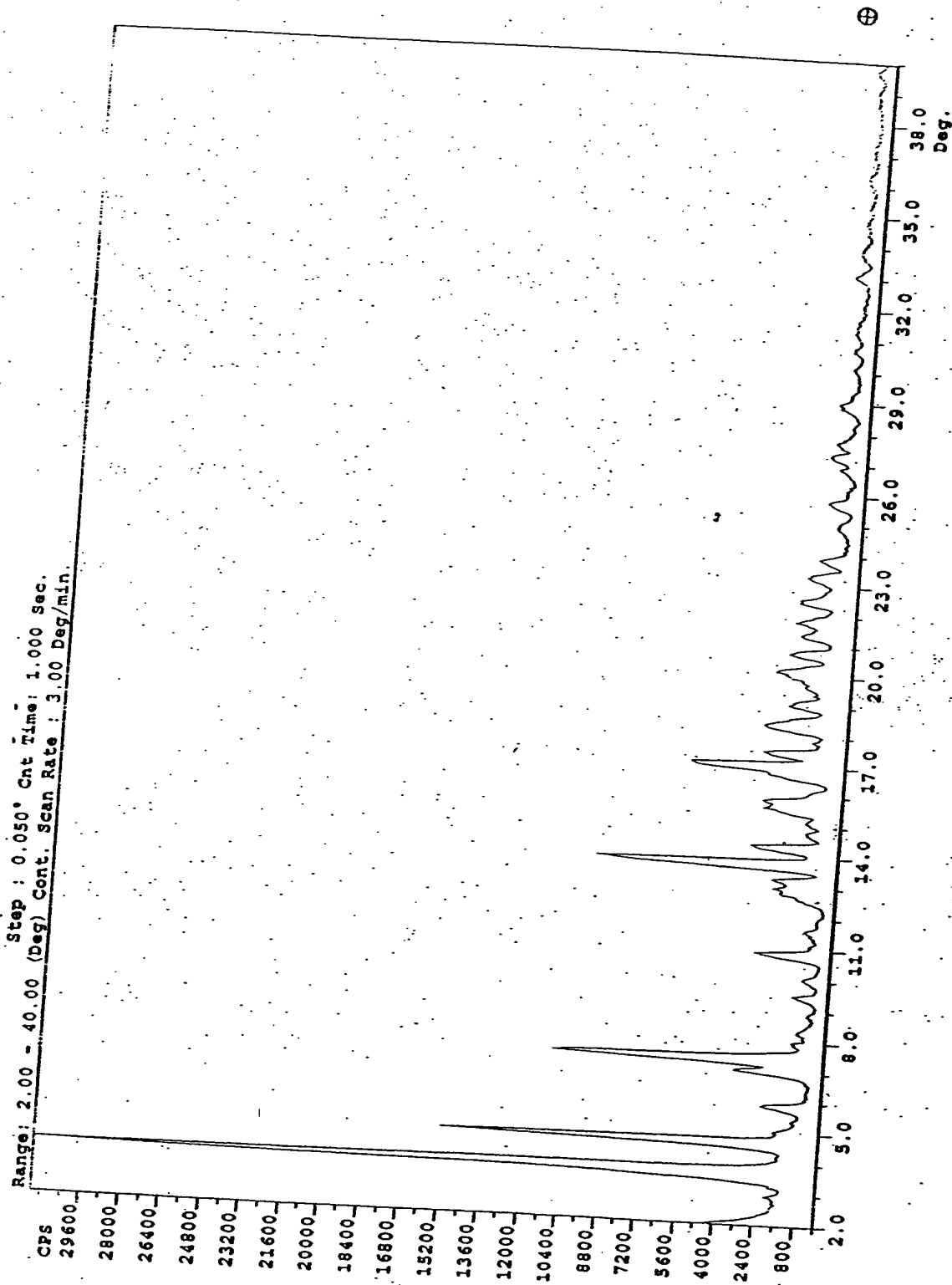


Fig. 18

V

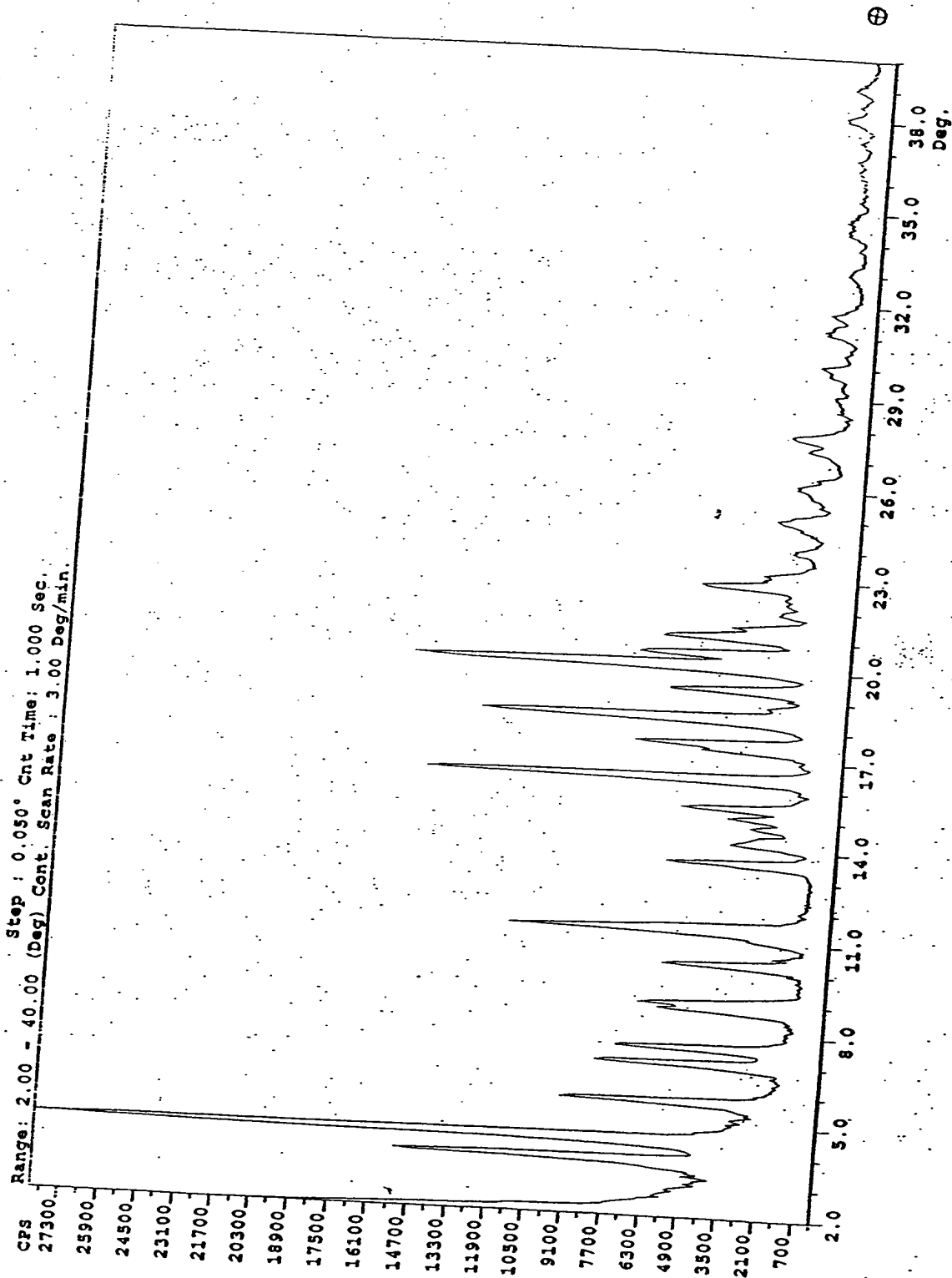


Fig 19  $\gamma$

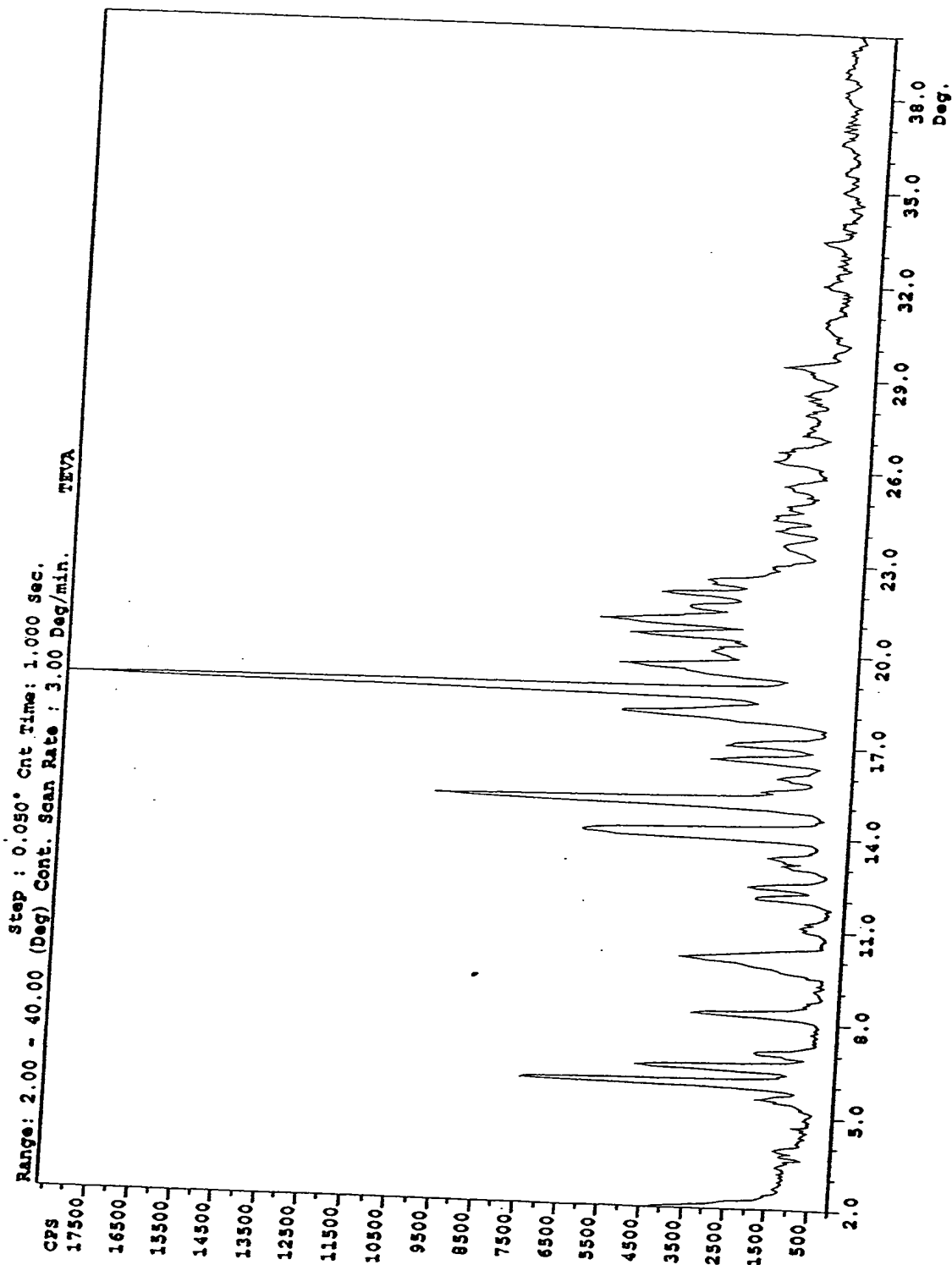


Figure 20 - Nateglinide Form Z

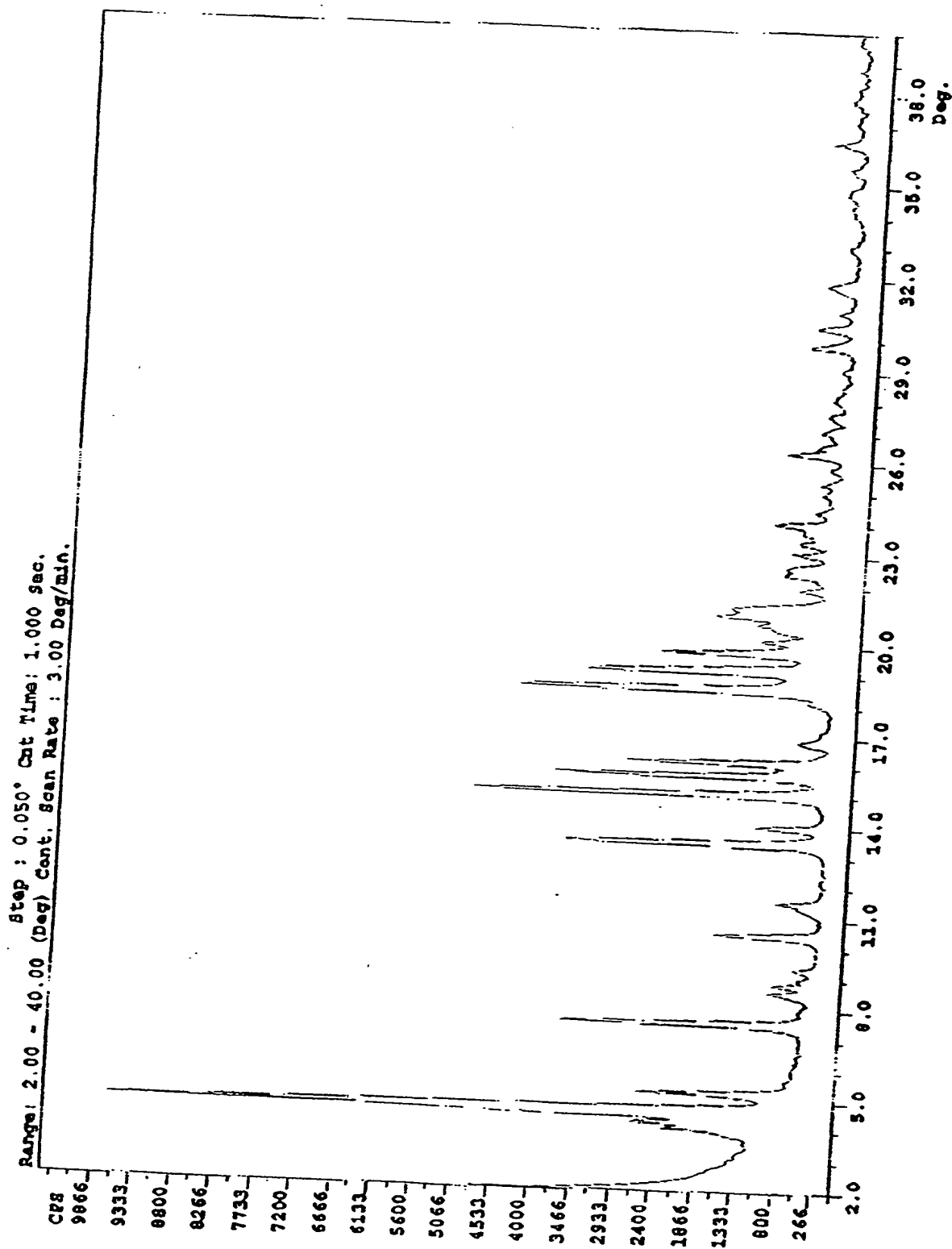


fig 2b x

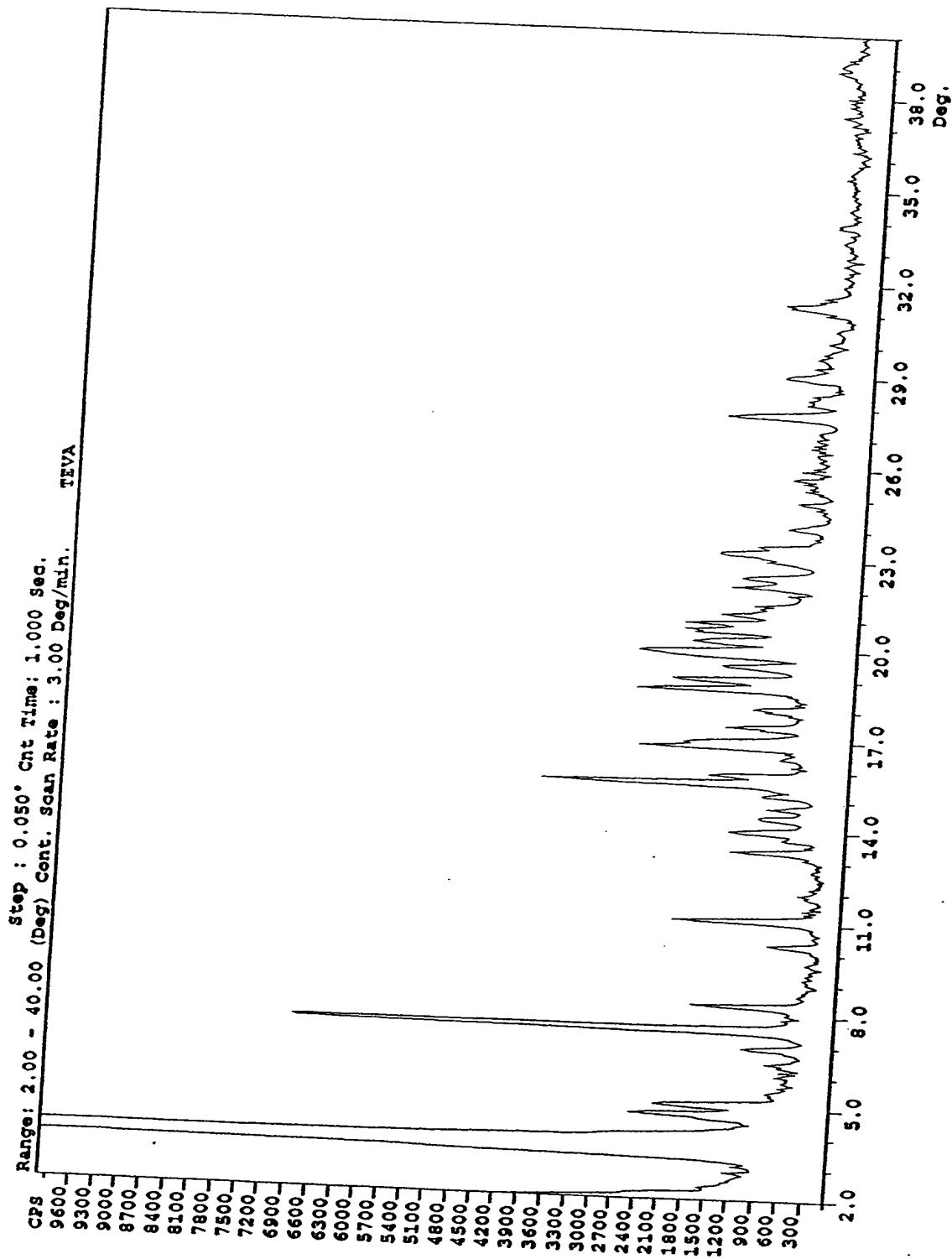


Fig. 2a B

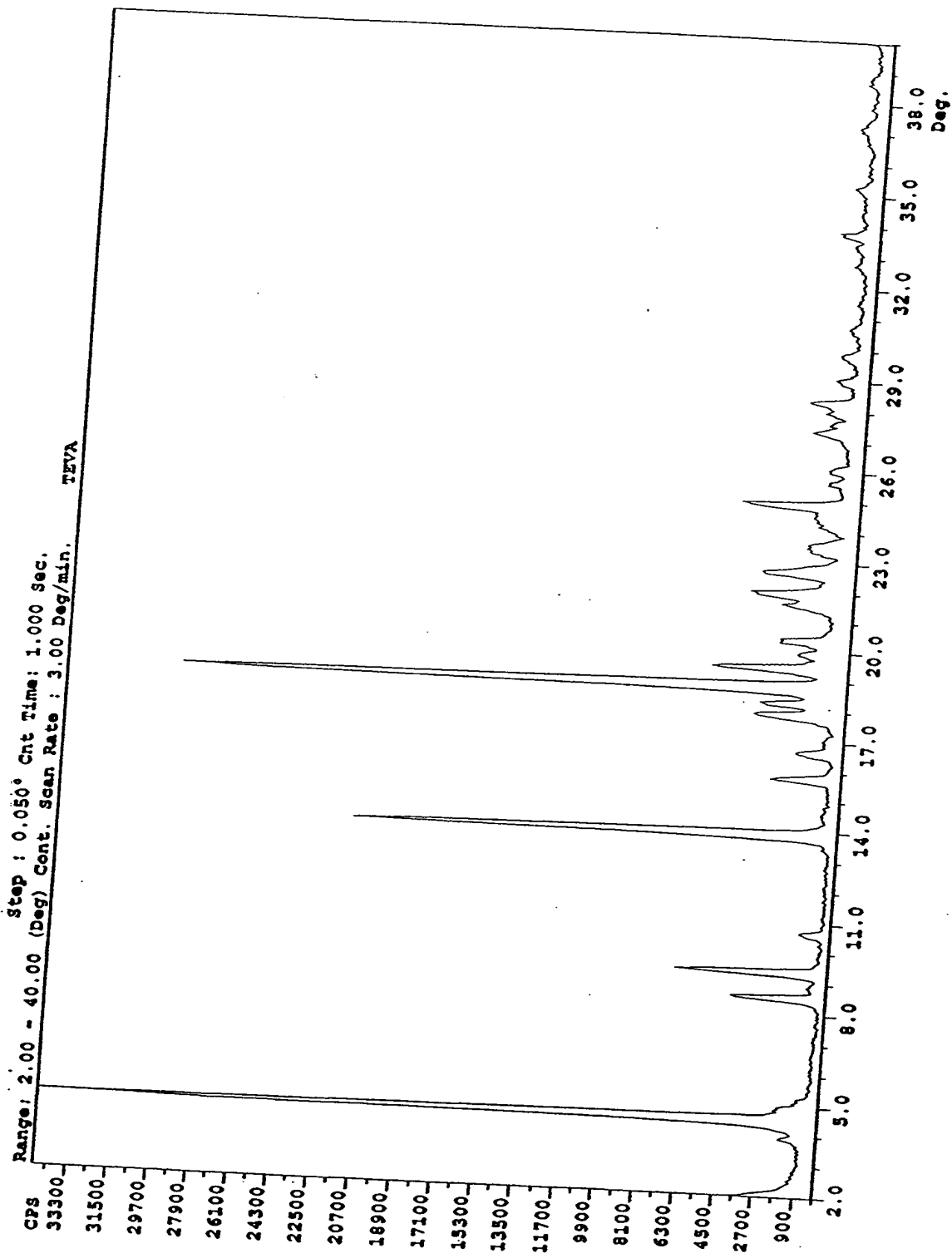


Fig 23 10

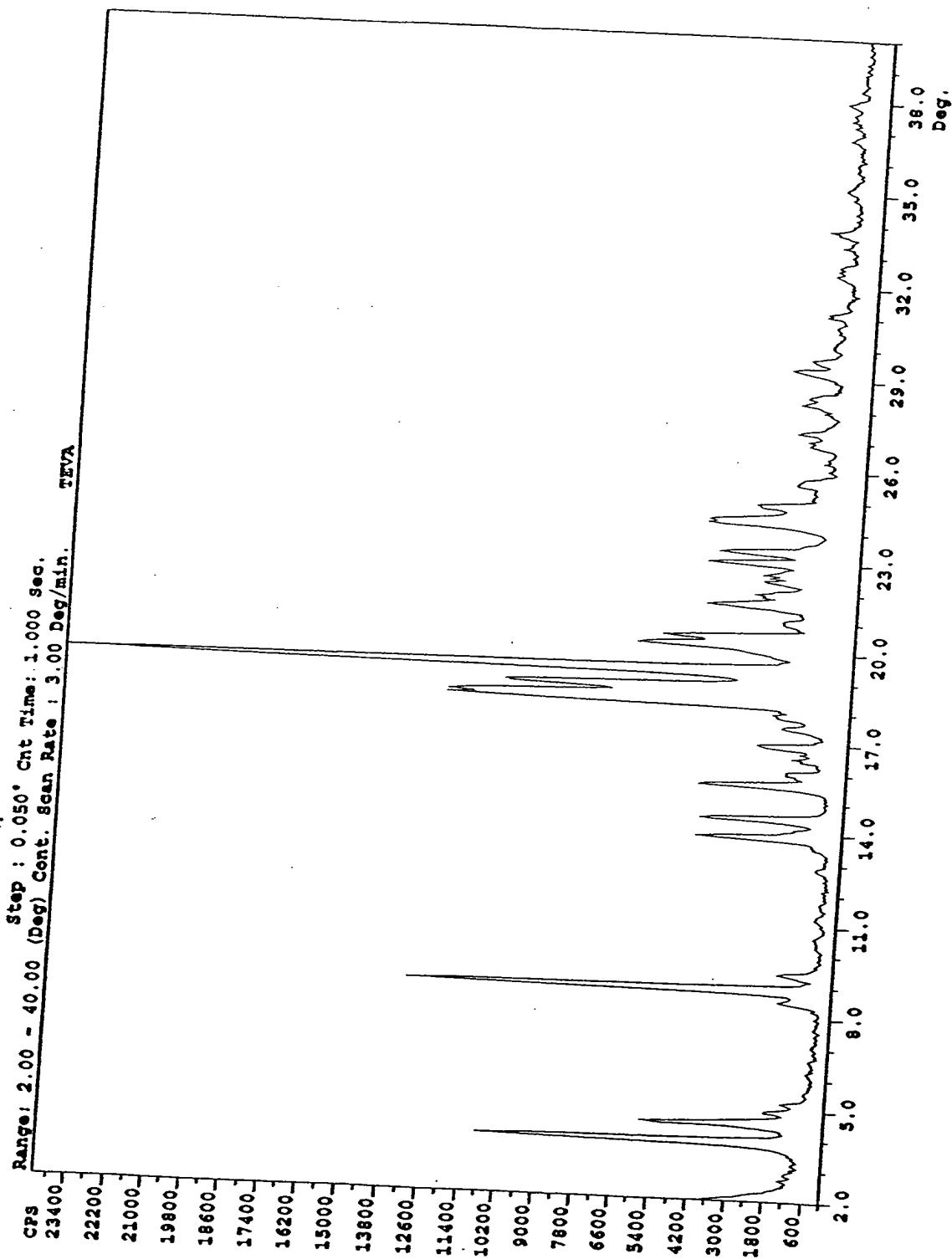


Fig 24

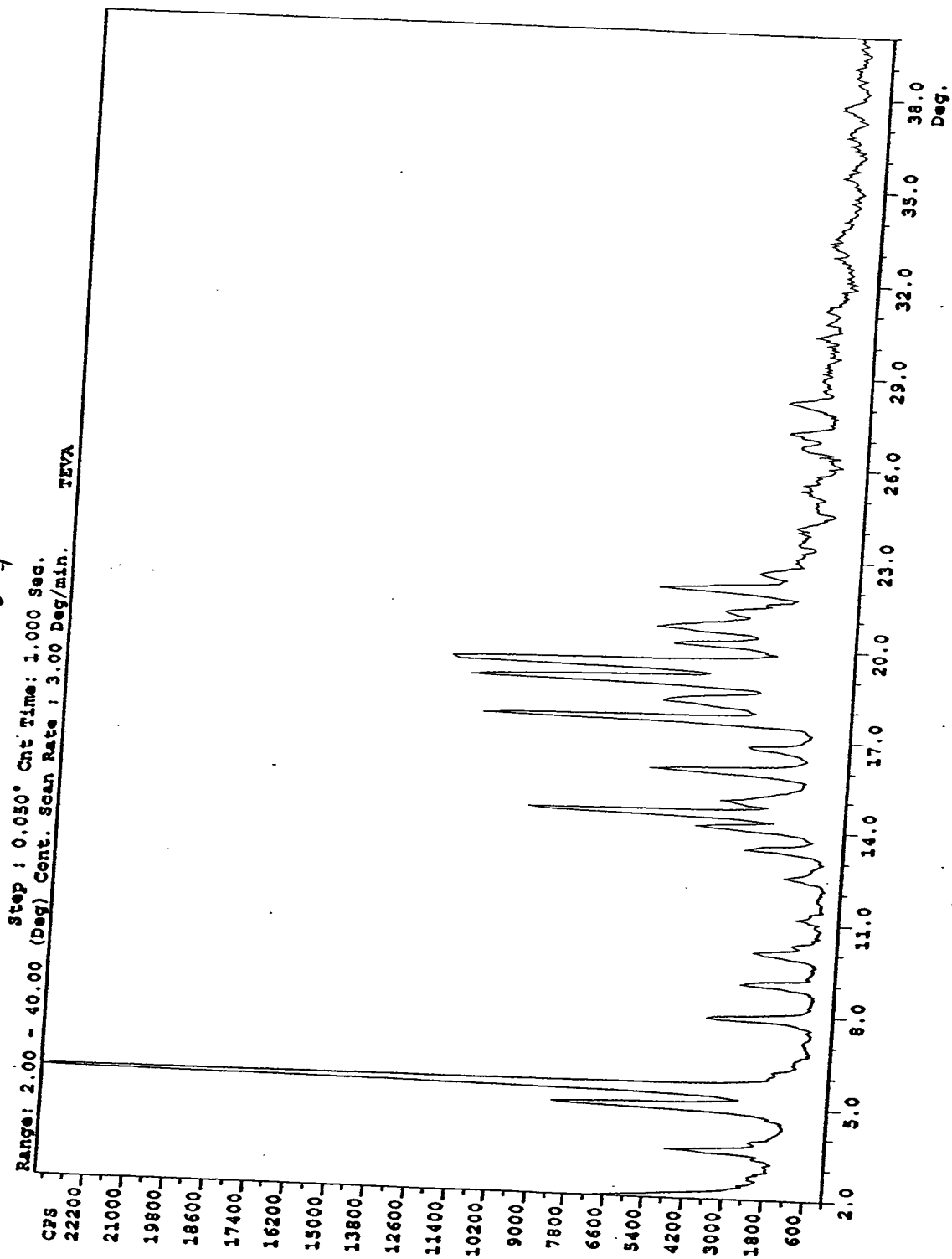




fig 25

E

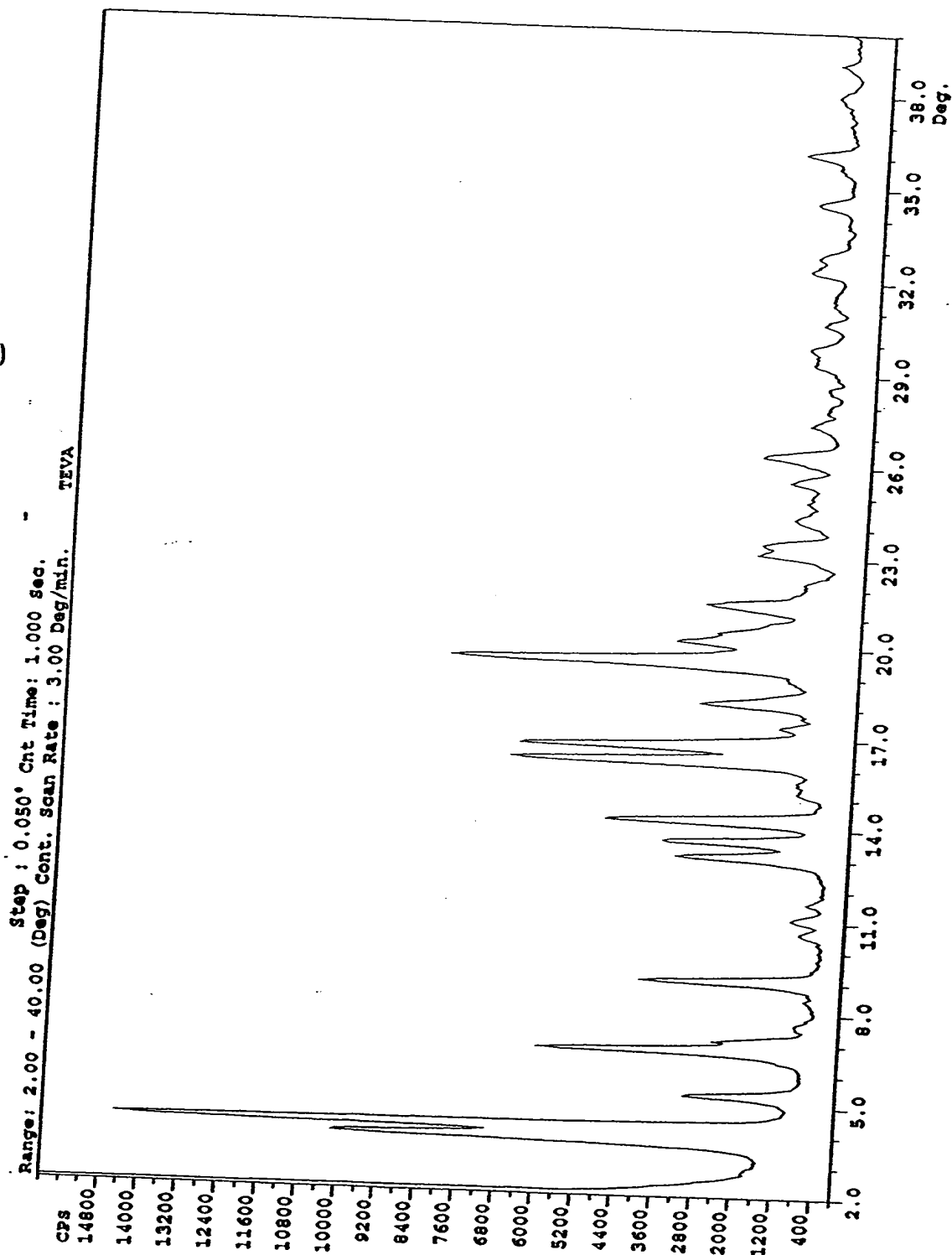
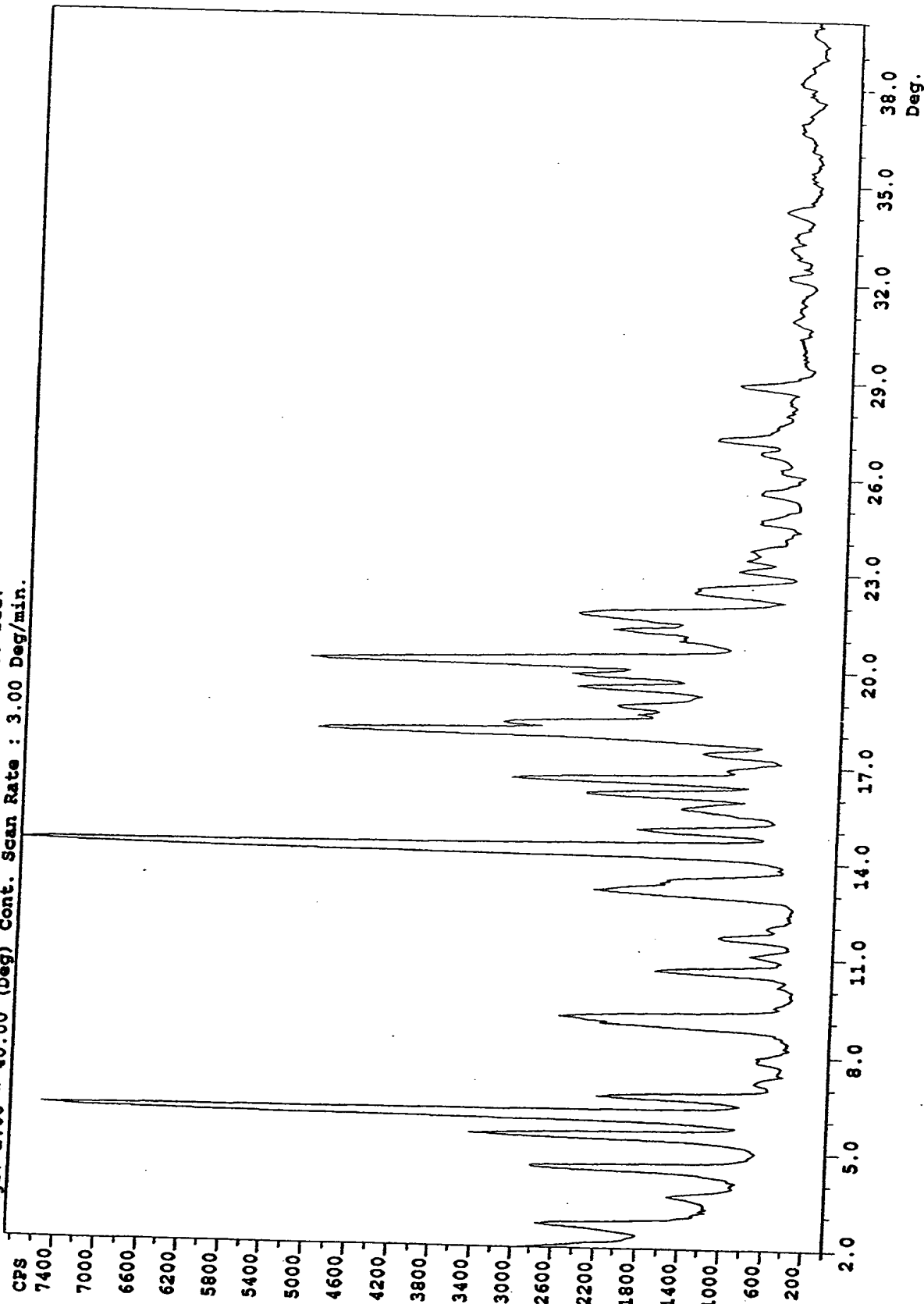


FIGURE 26

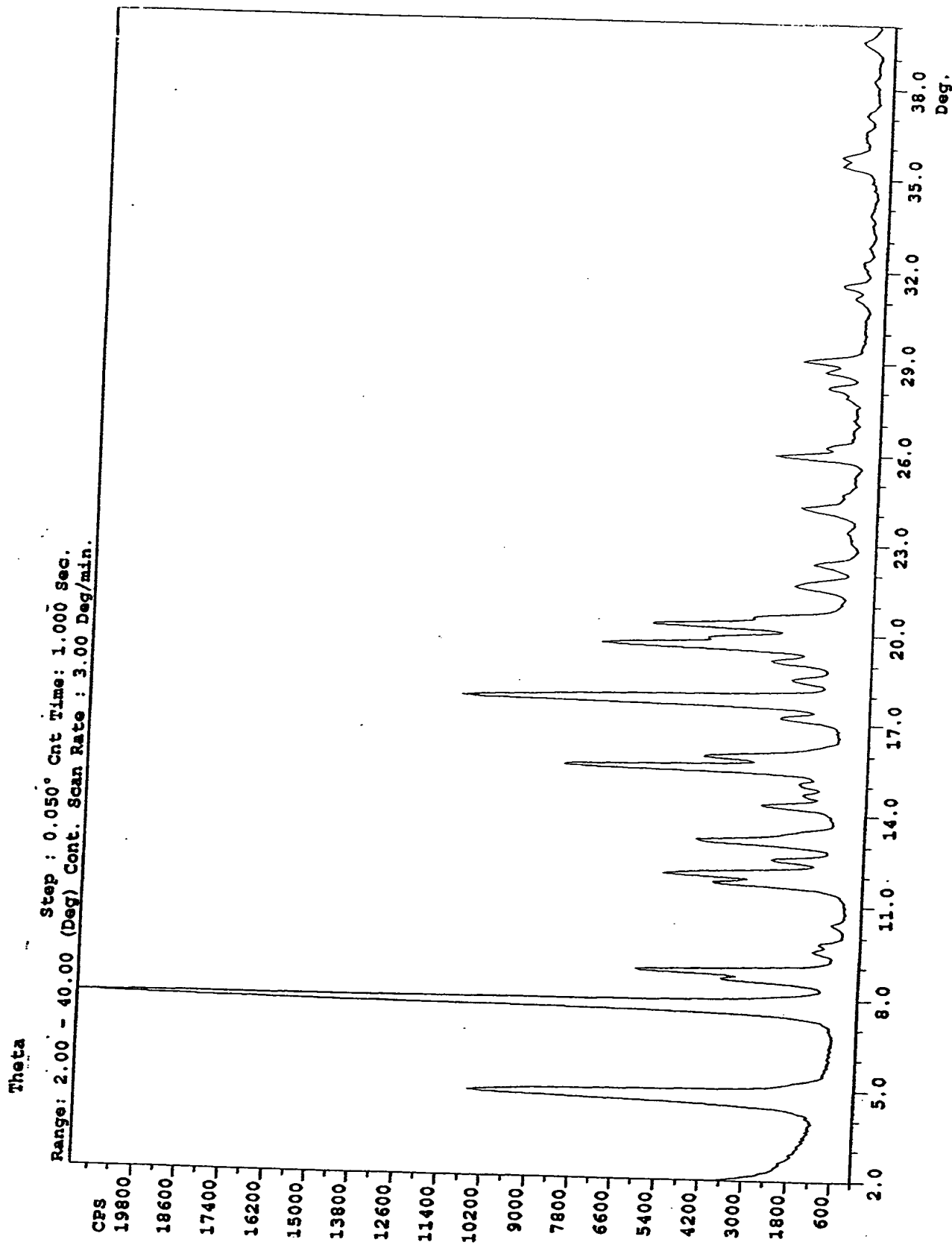
Sigma

Range: 2.00 - 40.00 (Deg) Cnt Time: 1.000 Sec.  
Step: 0.050° Cnt Rate: 3.00 Deg/min.



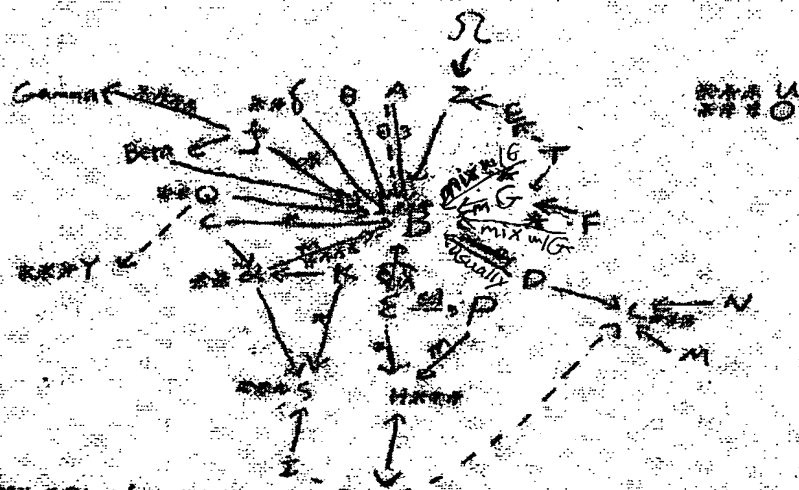
Form 2 (5)

FIGURE 28



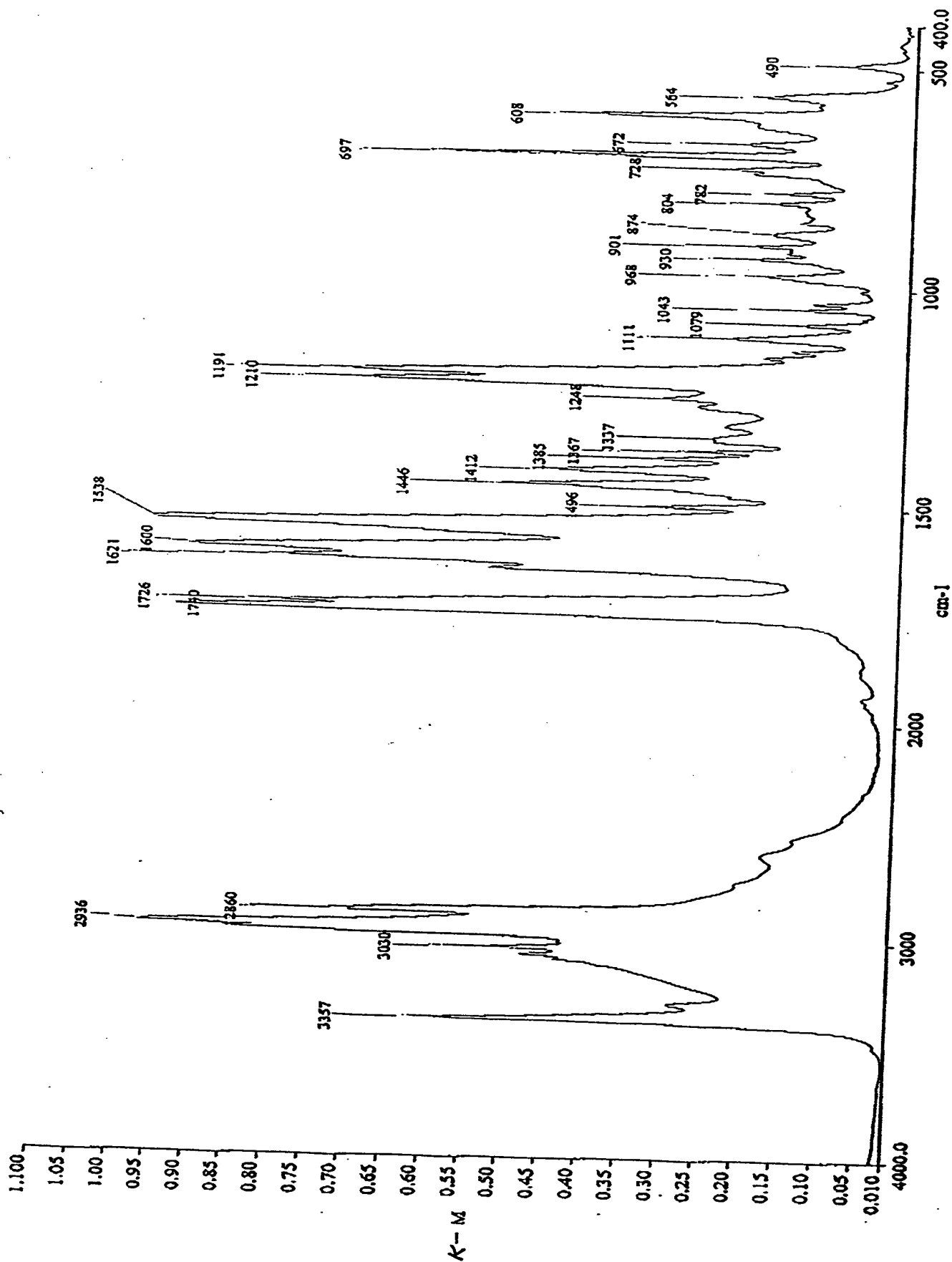
Form 8

Figure 28 - Thermal stability chart



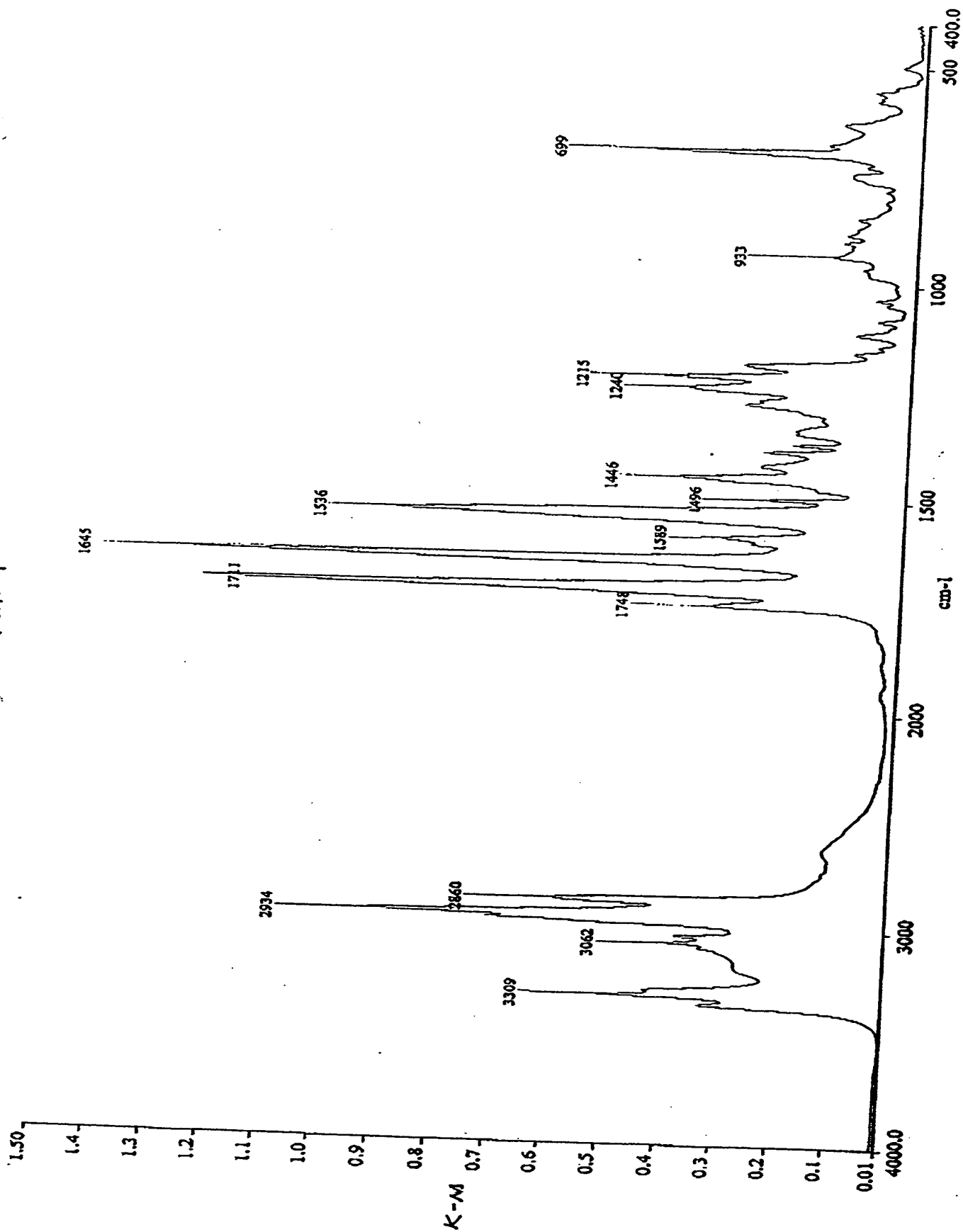
- \* Transformation may proceed through another form
- Thermally stable at lower heating temperatures ( $\sim 50^\circ\text{C}$ )
- Thermally stable forms
- Transformation after storage at room temperature in mixture with starting form.
- When starting material contains seeds.
- sol Results might vary depending on the solvate of Form Spriten used.

FIGURE 29  
Form



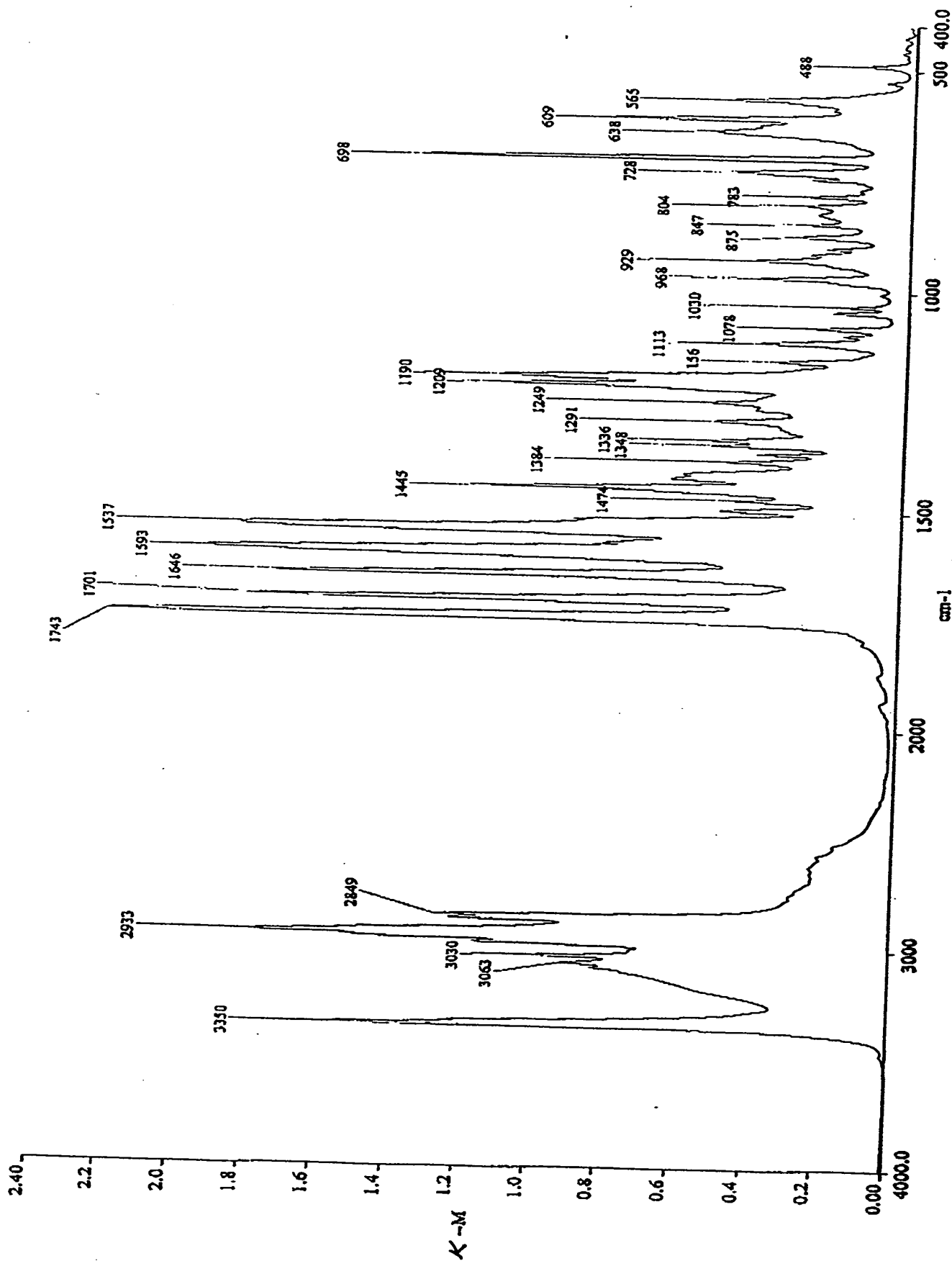
-DRIFT, 4000-400 CM-1, 16 scans, Resolution: 4.00cm-1

FIGURE 30  
-  $\bar{\nu}_{\text{cm}} \text{ } ^{\circ}\text{P}$



DRIFT, 4000-400  $\text{cm}^{-1}$ , 16 scans, Resolution: 4.00  $\text{cm}^{-1}$

FIGURE 30  
Form U



- DRIFT, 4000-400cm⁻¹, 16 scans, resolution: 4.0cm⁻¹

32  
 Figure 32 - Nateglinide Form Z

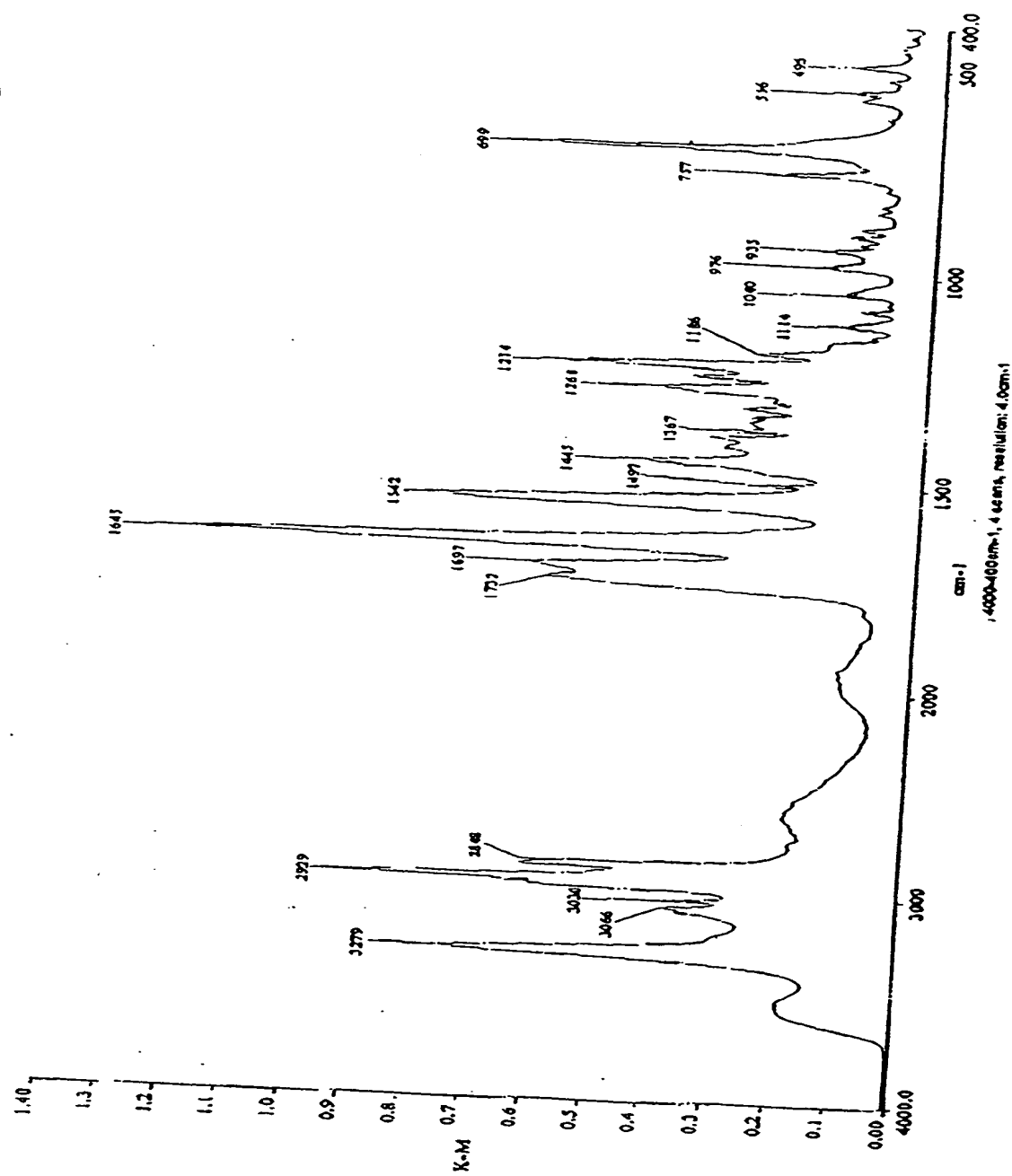




FIGURE 33  
Form α

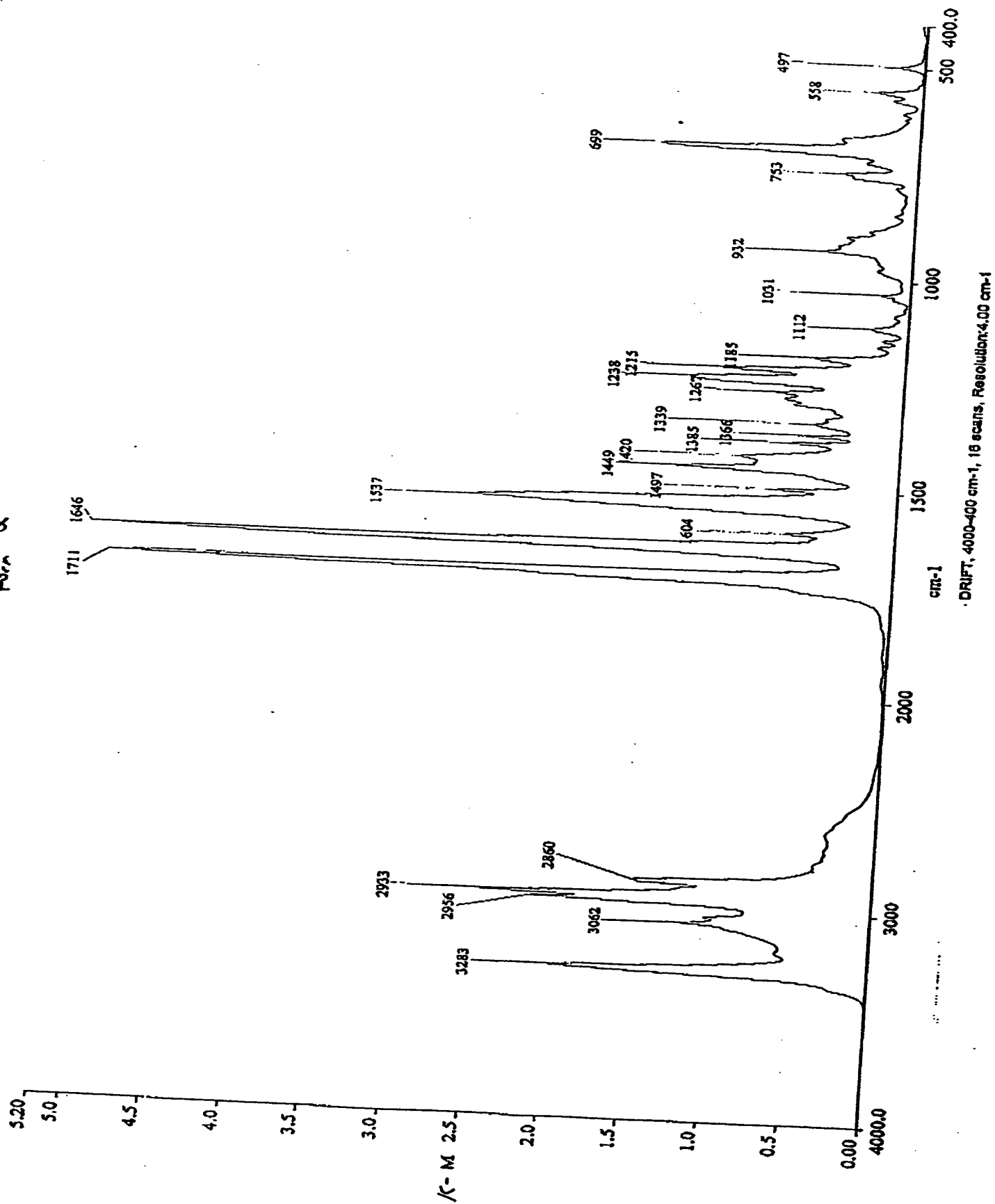
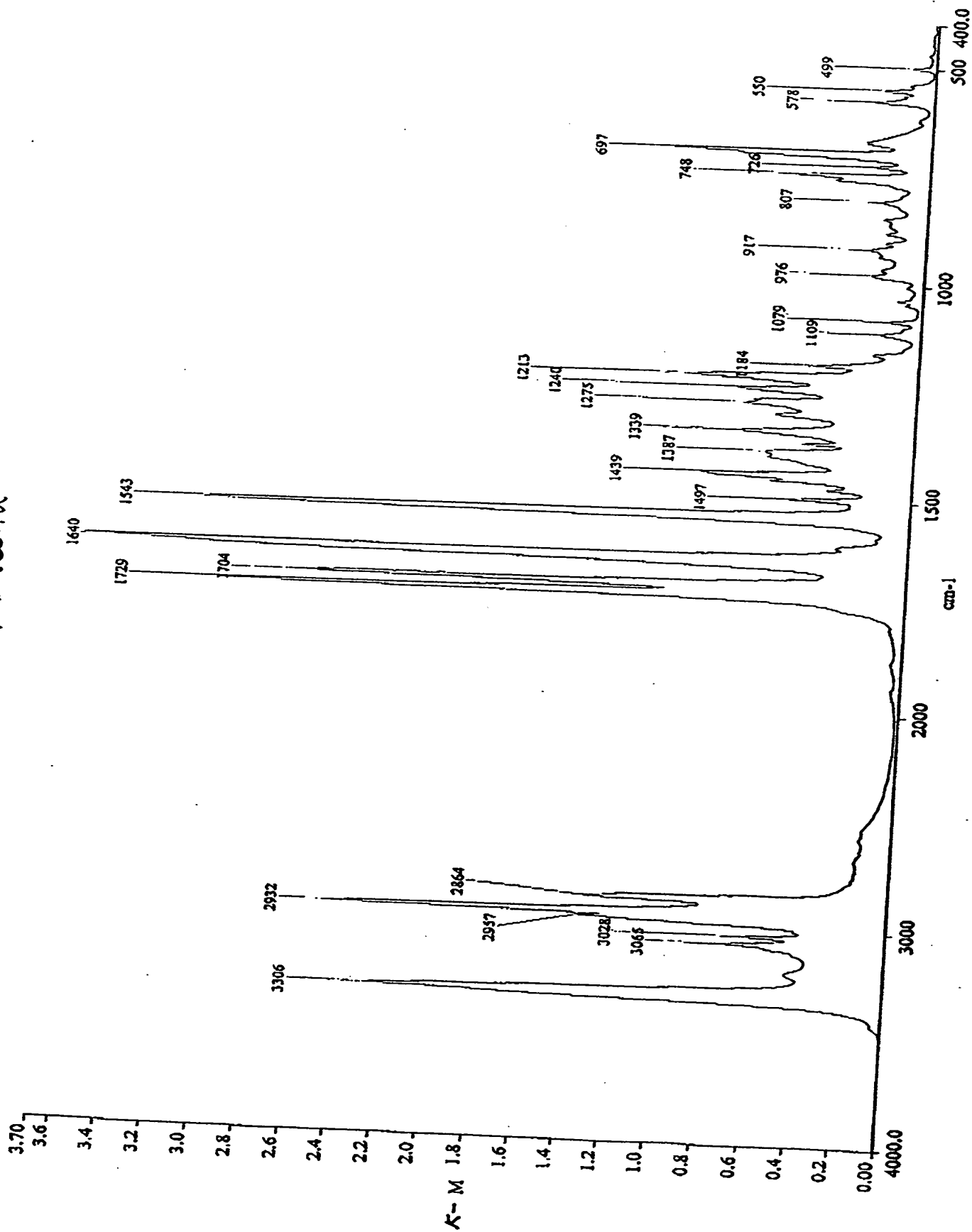


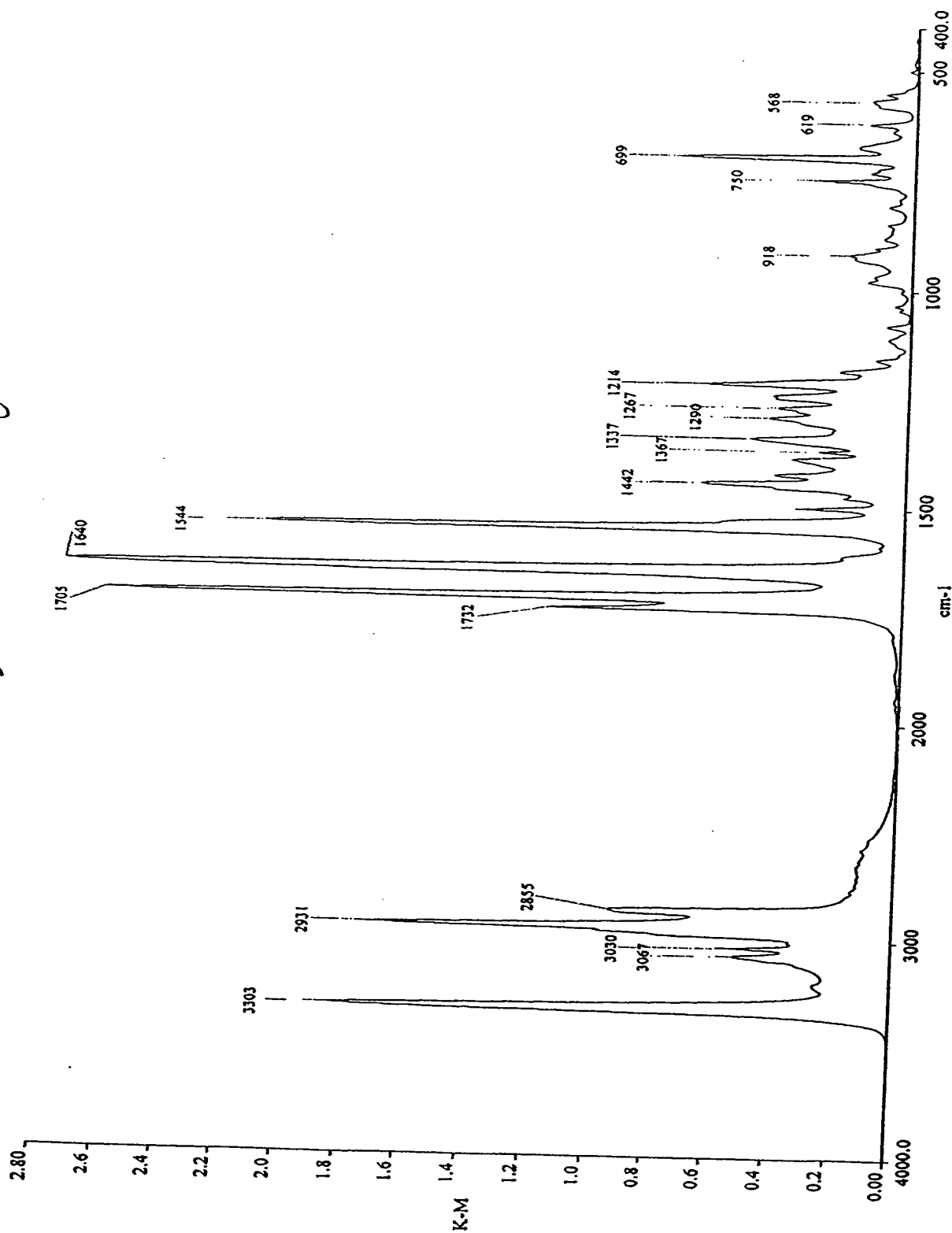
FIGURE 34 Form delta



DRIFT, 4000-400cm⁻¹, 16 scans, resolution: 4.0cm⁻¹

FIGURE 35

- form



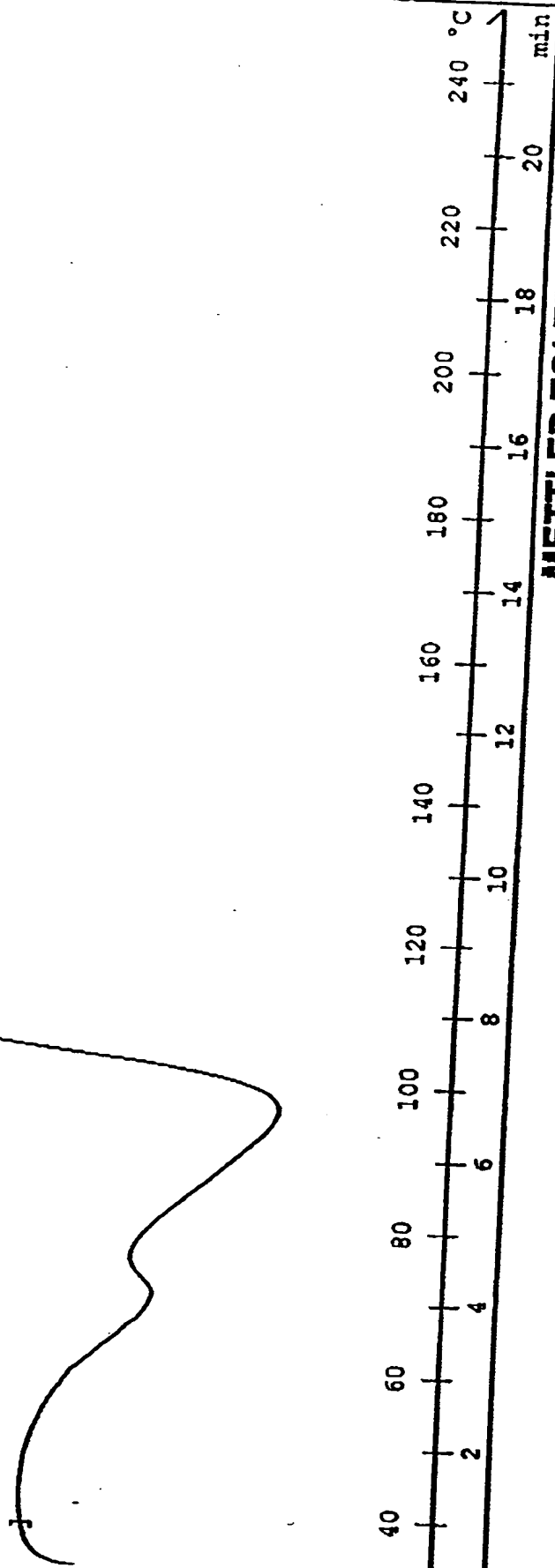
DRIFT, 4000-400 $\text{cm}^{-1}$ , 16 SCANS RESOLUTION: 4.0 $\text{cm}^{-1}$

form (O)

FIGURE 36

Form A

Method: 30-250°C, 10°C/min, 40ml/min N<sub>2</sub>  
30.0-250.0°C 10.00°C/min N<sub>2</sub>, 40.0 ml/min



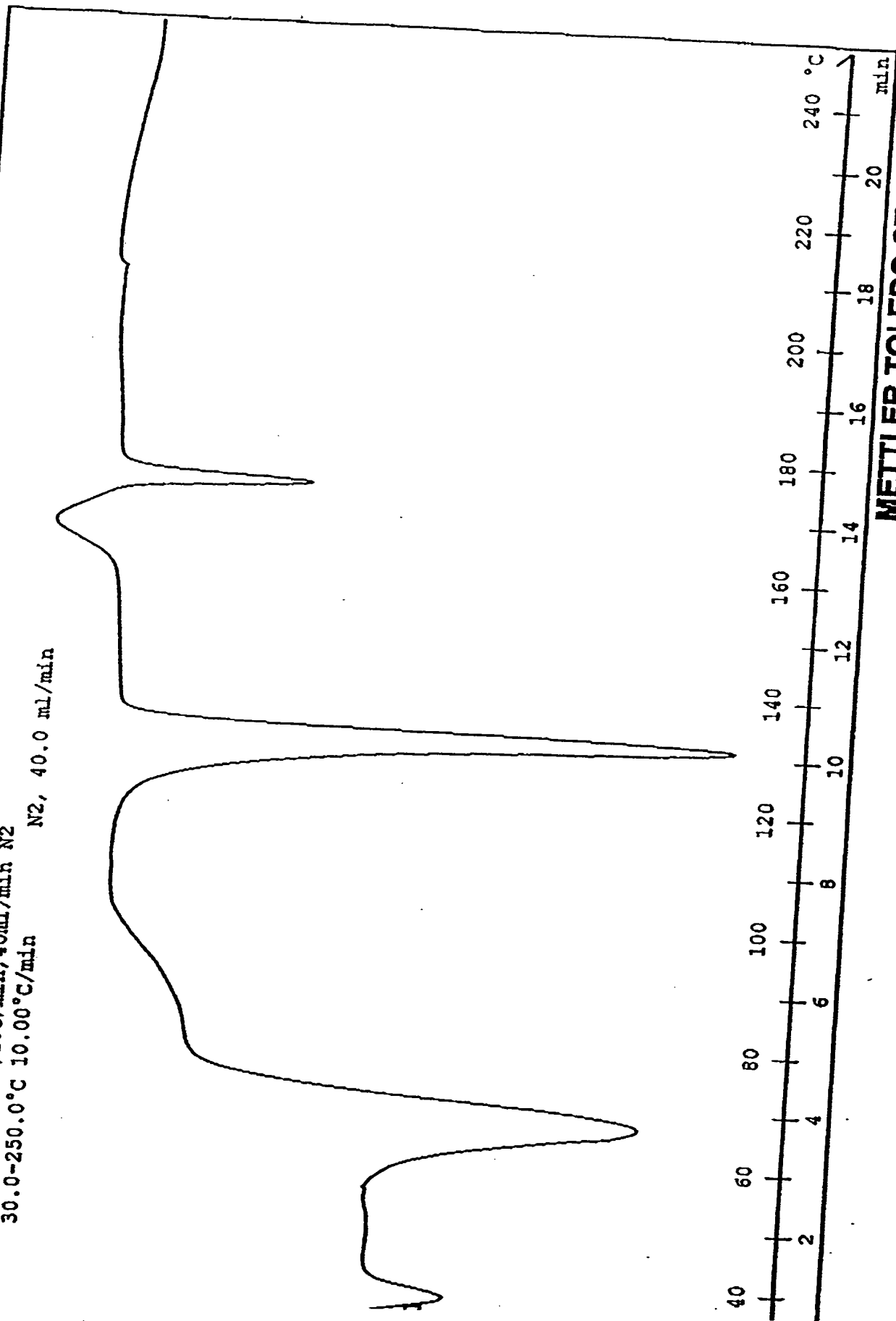
METTLER TOLEDO STAR® System

FIGURE 37

Form D

Method: 30-250°C, 10°C/min, 40ml/min N<sub>2</sub>  
30.0-250.0°C 10.00°C/min

N<sub>2</sub>, 40.0 ml/min



METTLER TOLEDO STAR® System

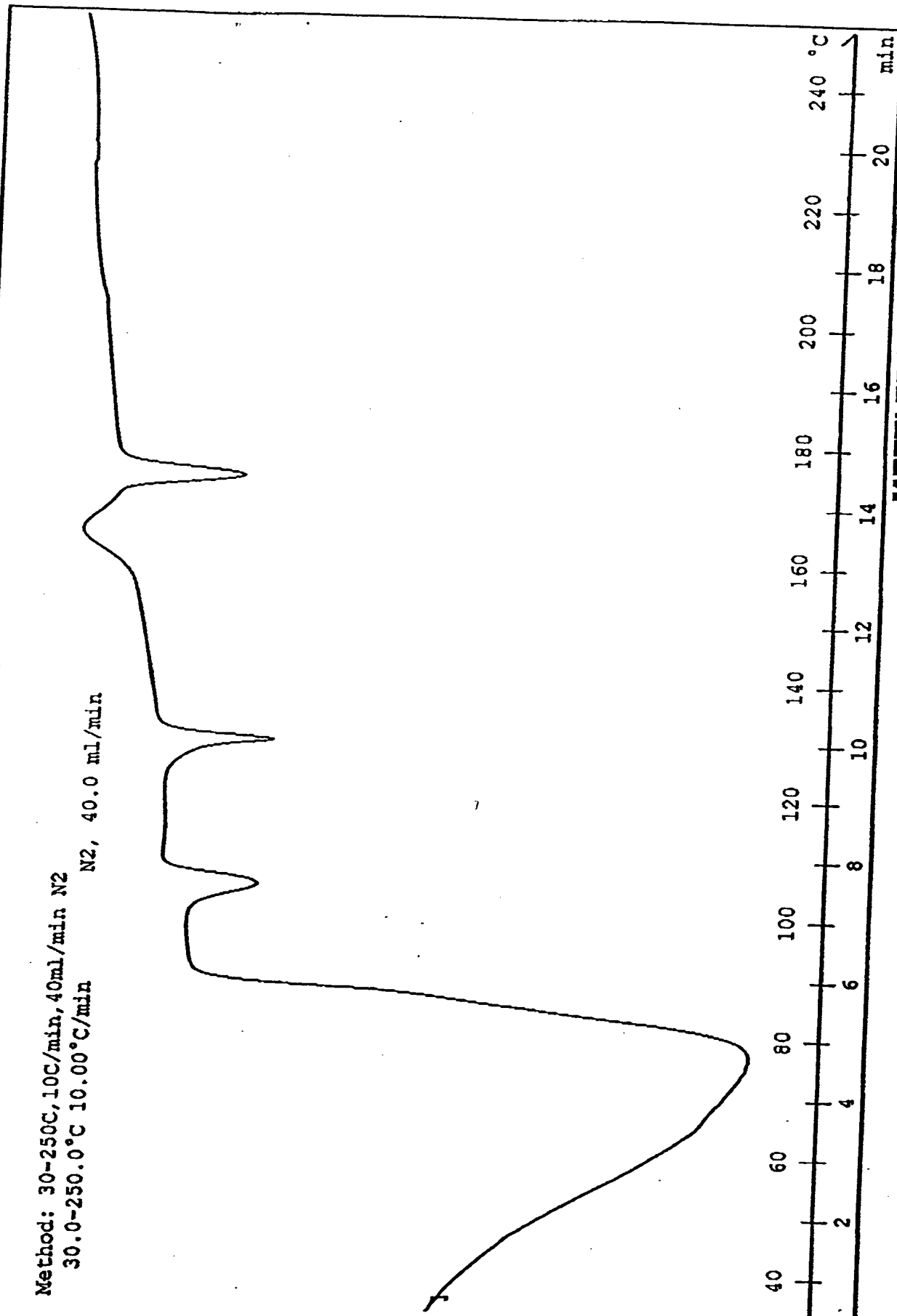
FIGURE 38

Form E

Method: 30-250°C, 10°C/min, 40ml/min N<sub>2</sub>

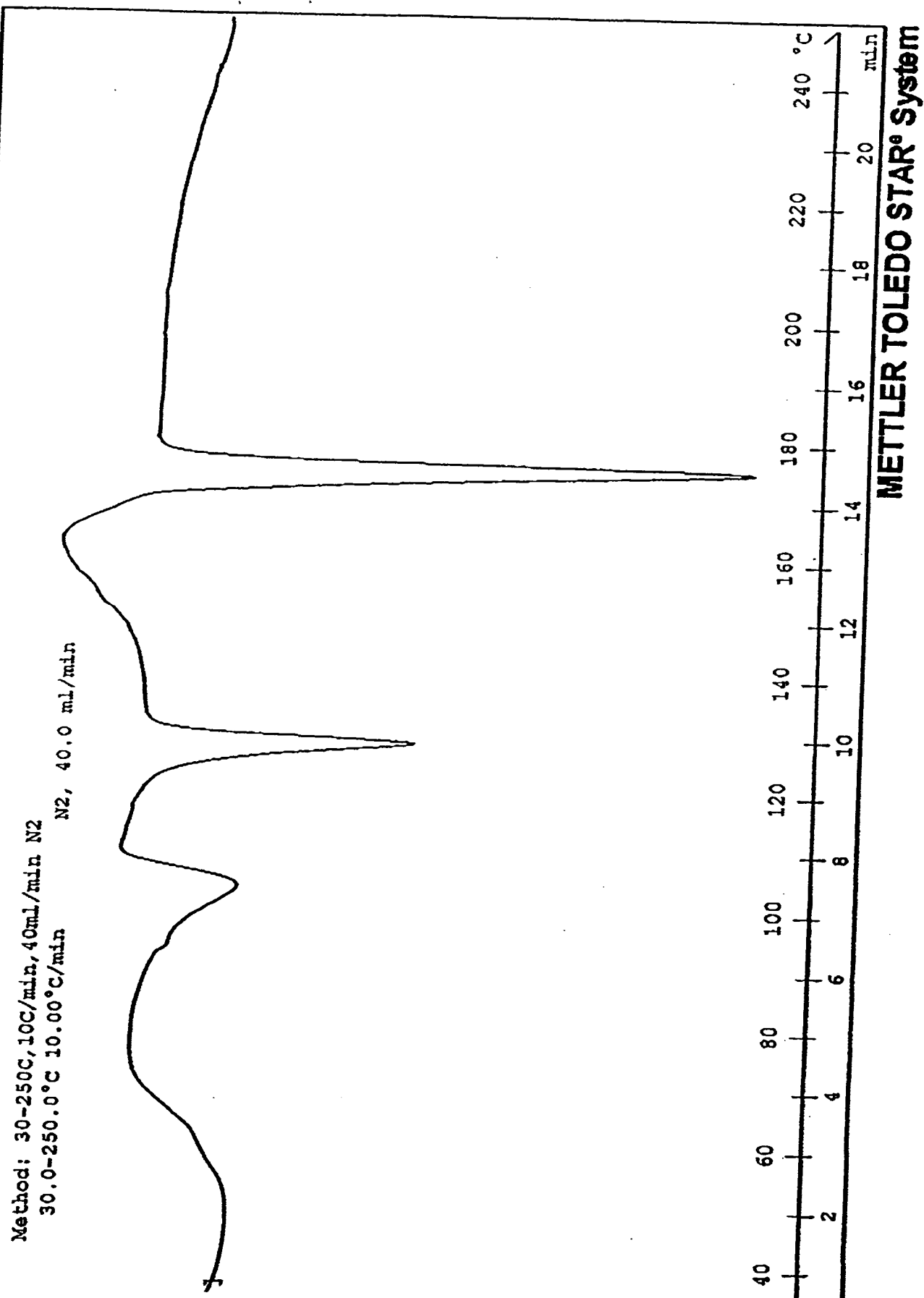
30.0-250.0°C 10.00°C/min

N<sub>2</sub>, 40.0 ml/min



METTLER TOLEDO STAR® System

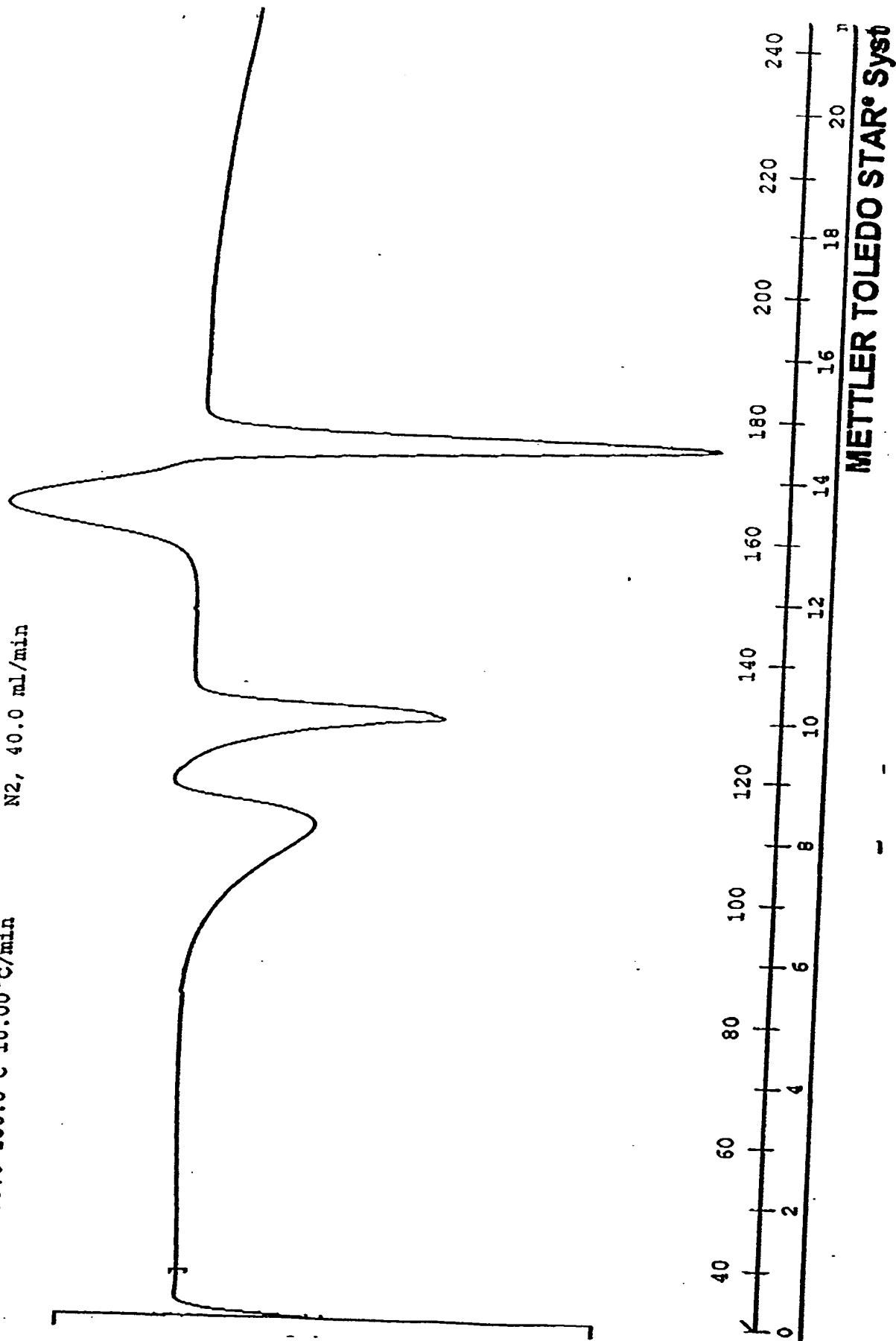
39  
FIGURE 1



40  
FIGURE 83

IXO

Method: 30-250C, 10C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® Syst



FIGURE 2091

Form I

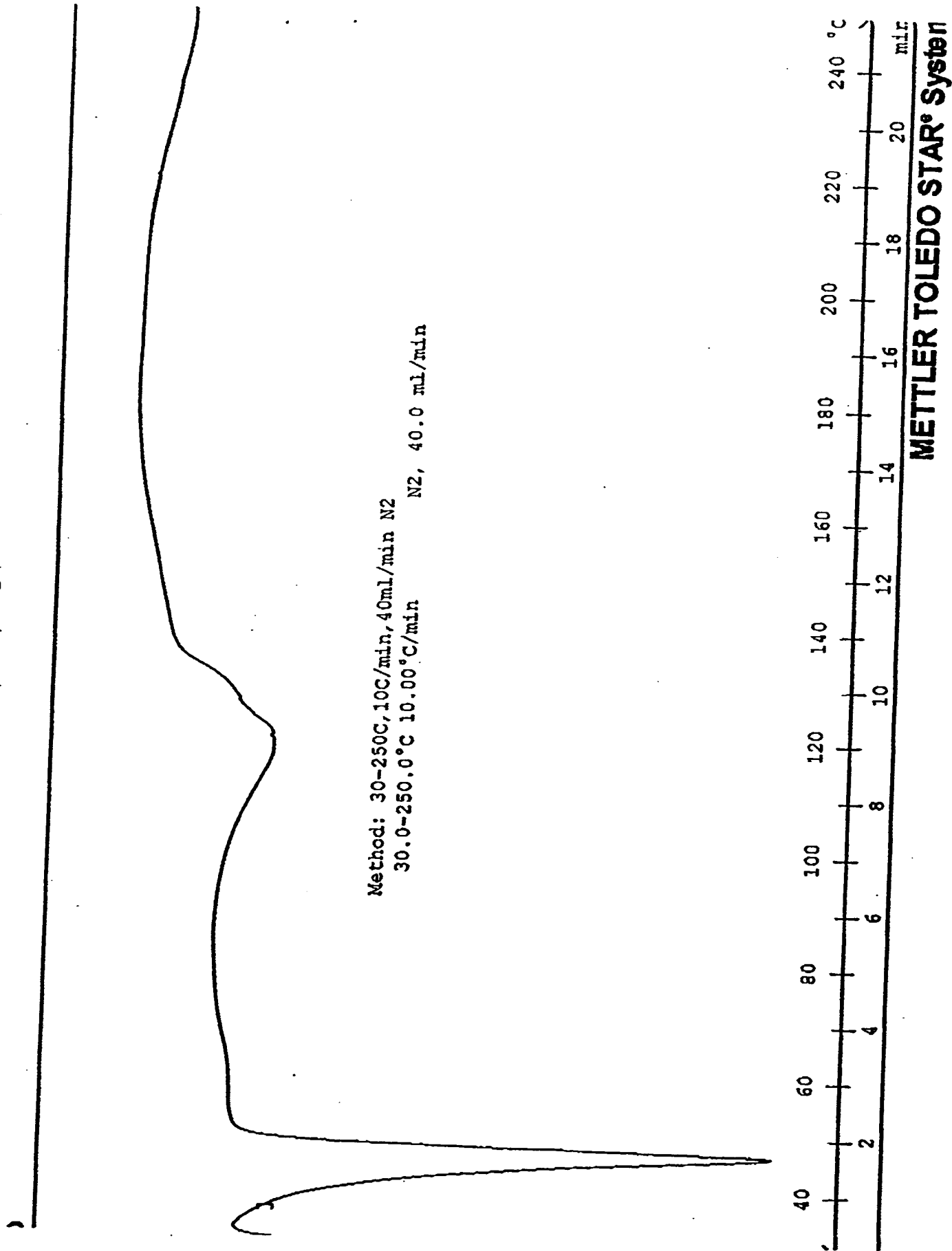


FIGURE 4a  
Form J

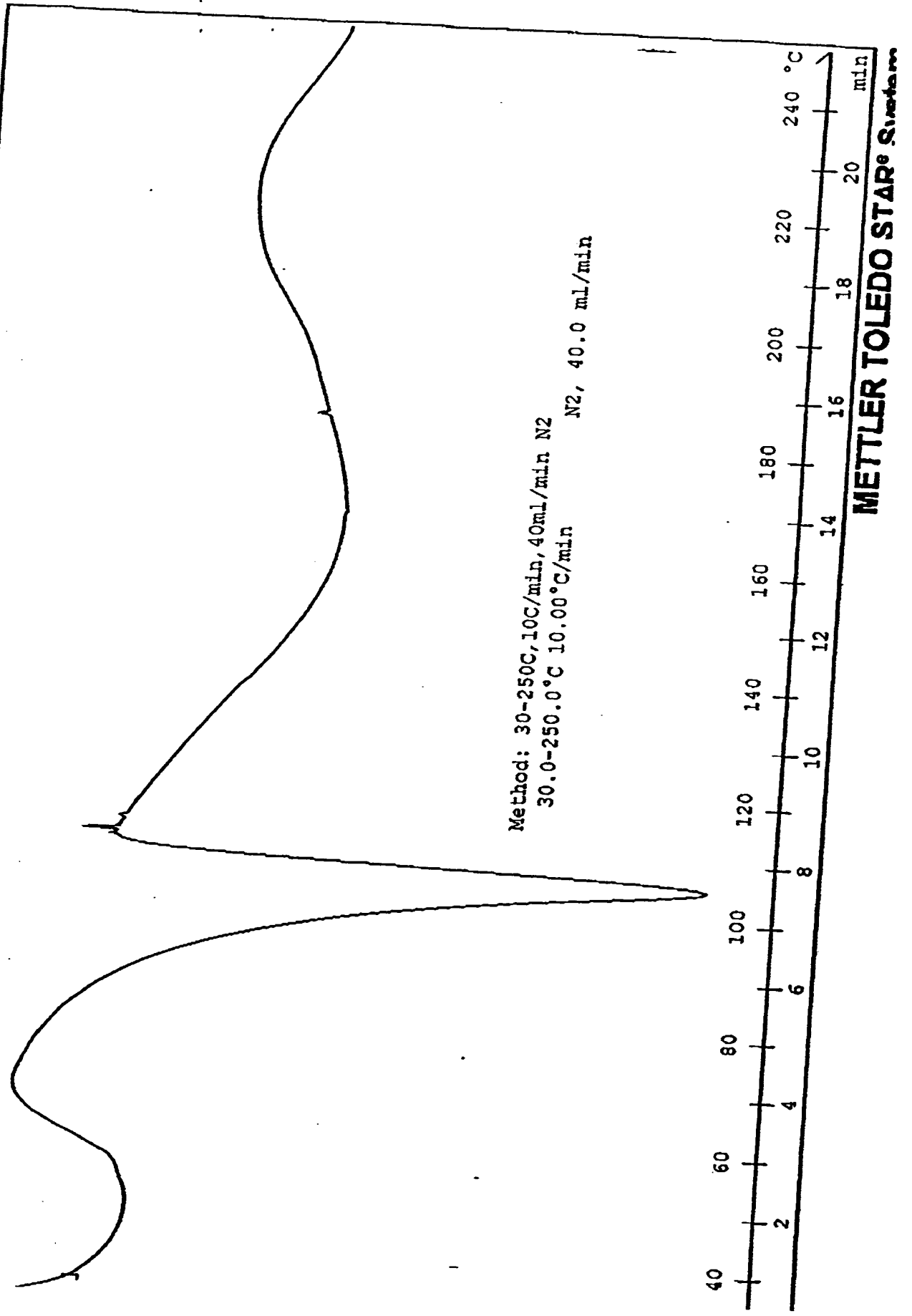


FIGURE 43  
Form K

Method: 30-250°C, 10°C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min  
N2, 40.0 ml/min

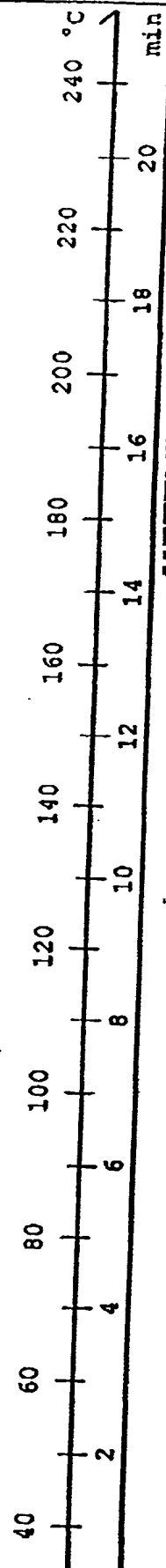
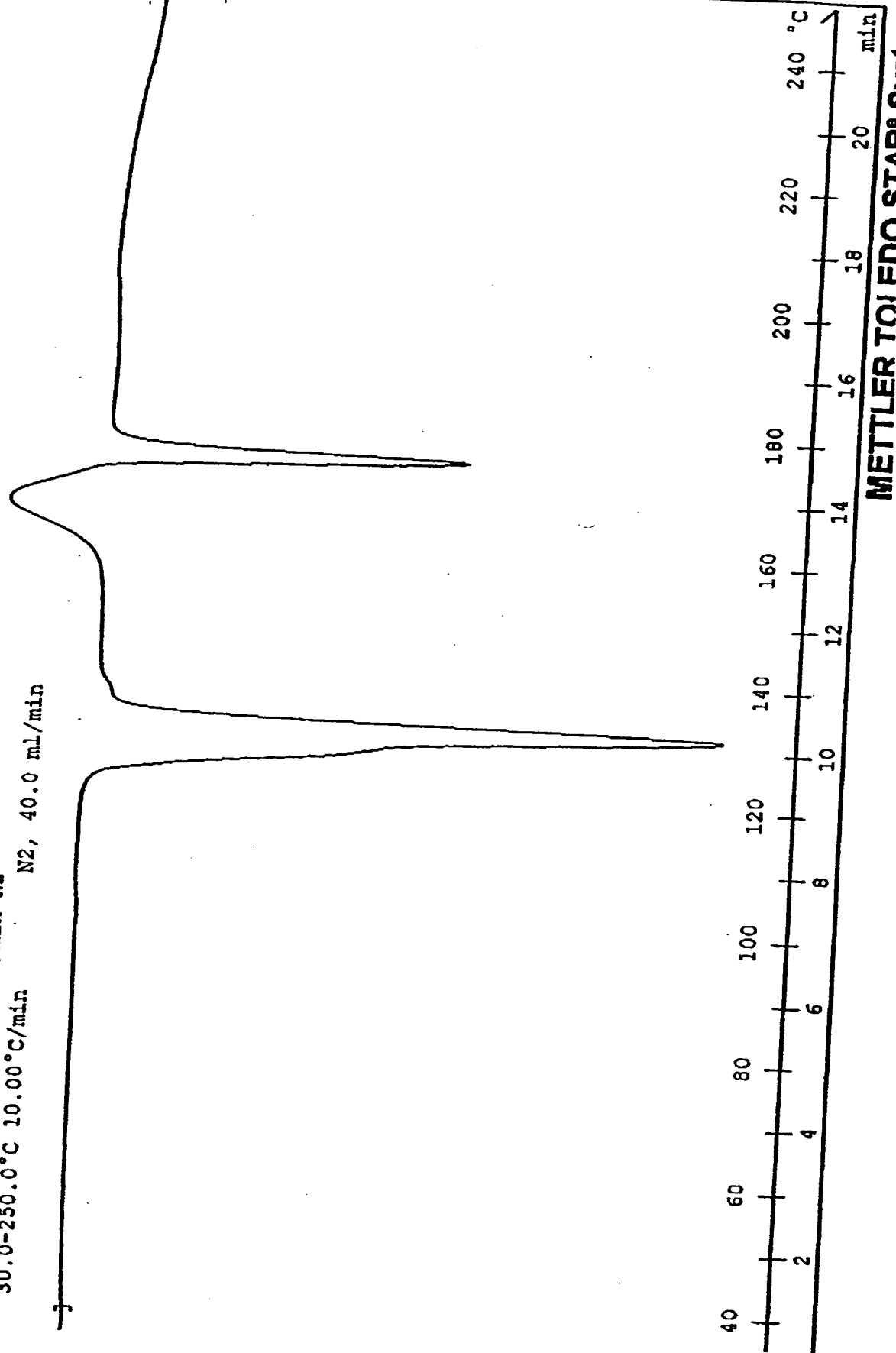


FIGURE 42 4/4  
Form L

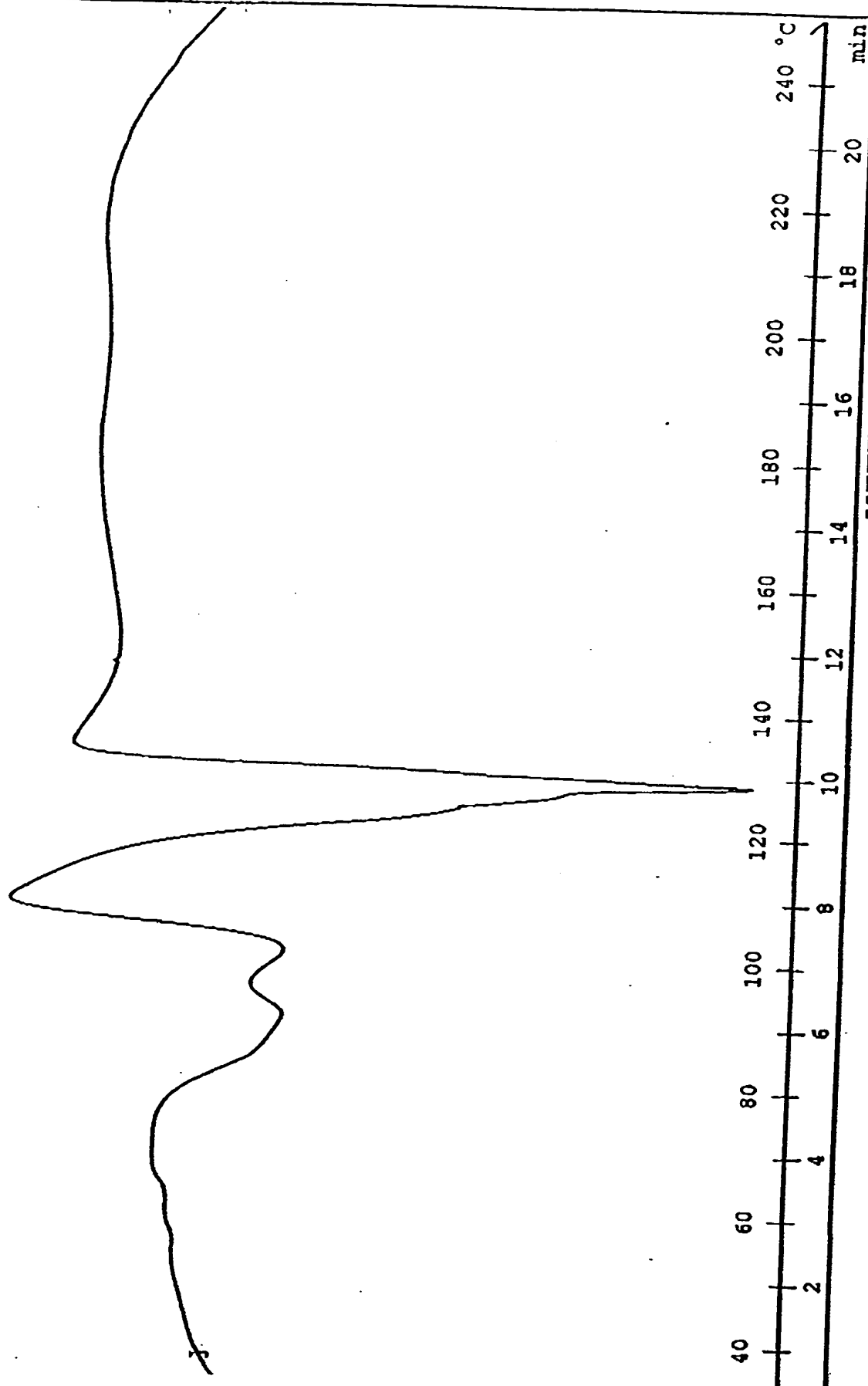
Method: 30-250°C, 10°C/min, 40 ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STABO 6.1.1.1

FIGURE 45  
Form M

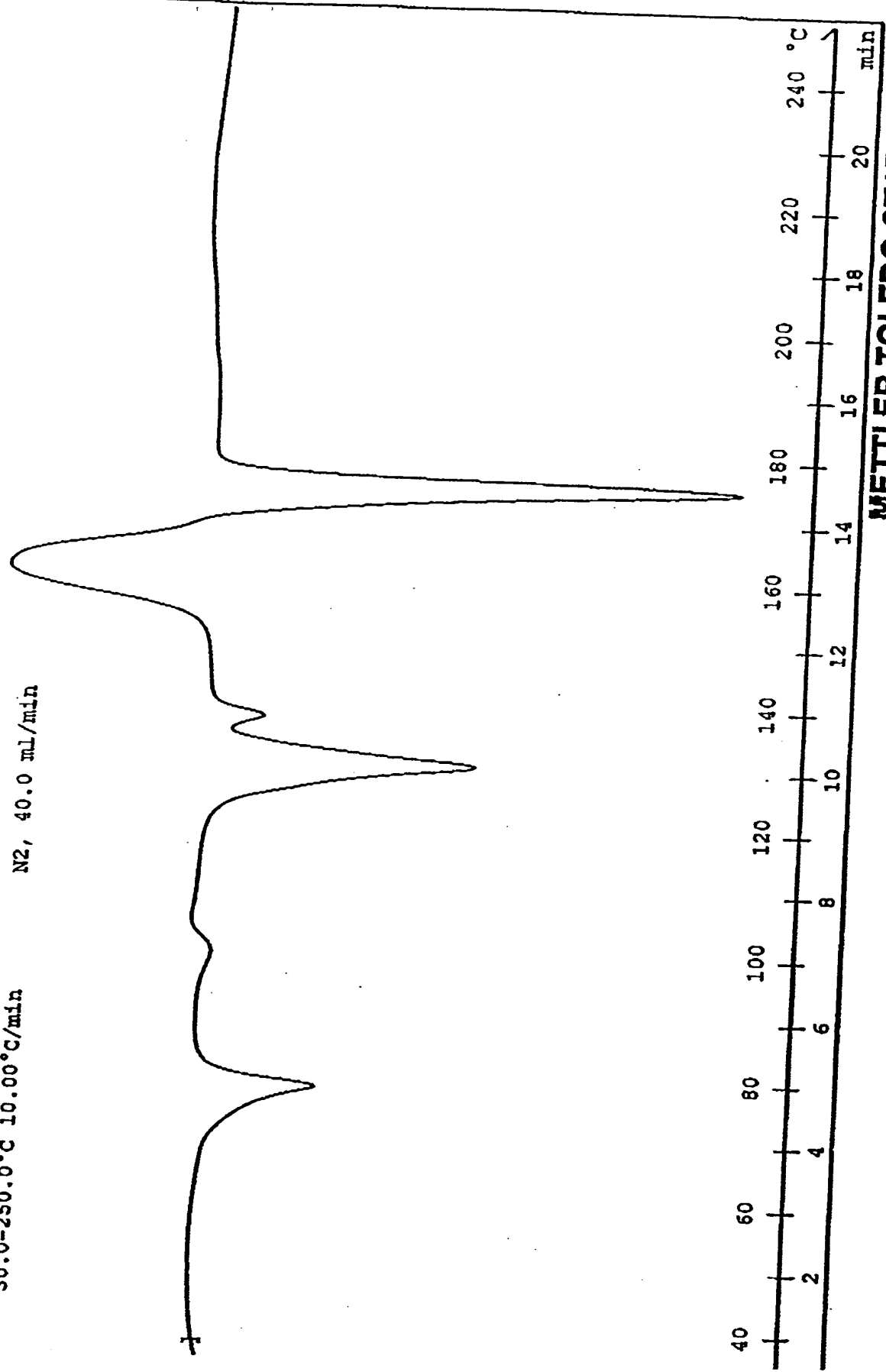
Method: 30-250°C, 10°C/min, 40 ml/min N<sub>2</sub>  
30.0-250.0°C 10.00°C/min



METTLER TOLEDO STAR® System

FIGURE 44 46  
Form N

Method: 30-250C, 10C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE #5 47  
Form G

Method: 30-250°C, 10°C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min

N2, 40.0 ml/min

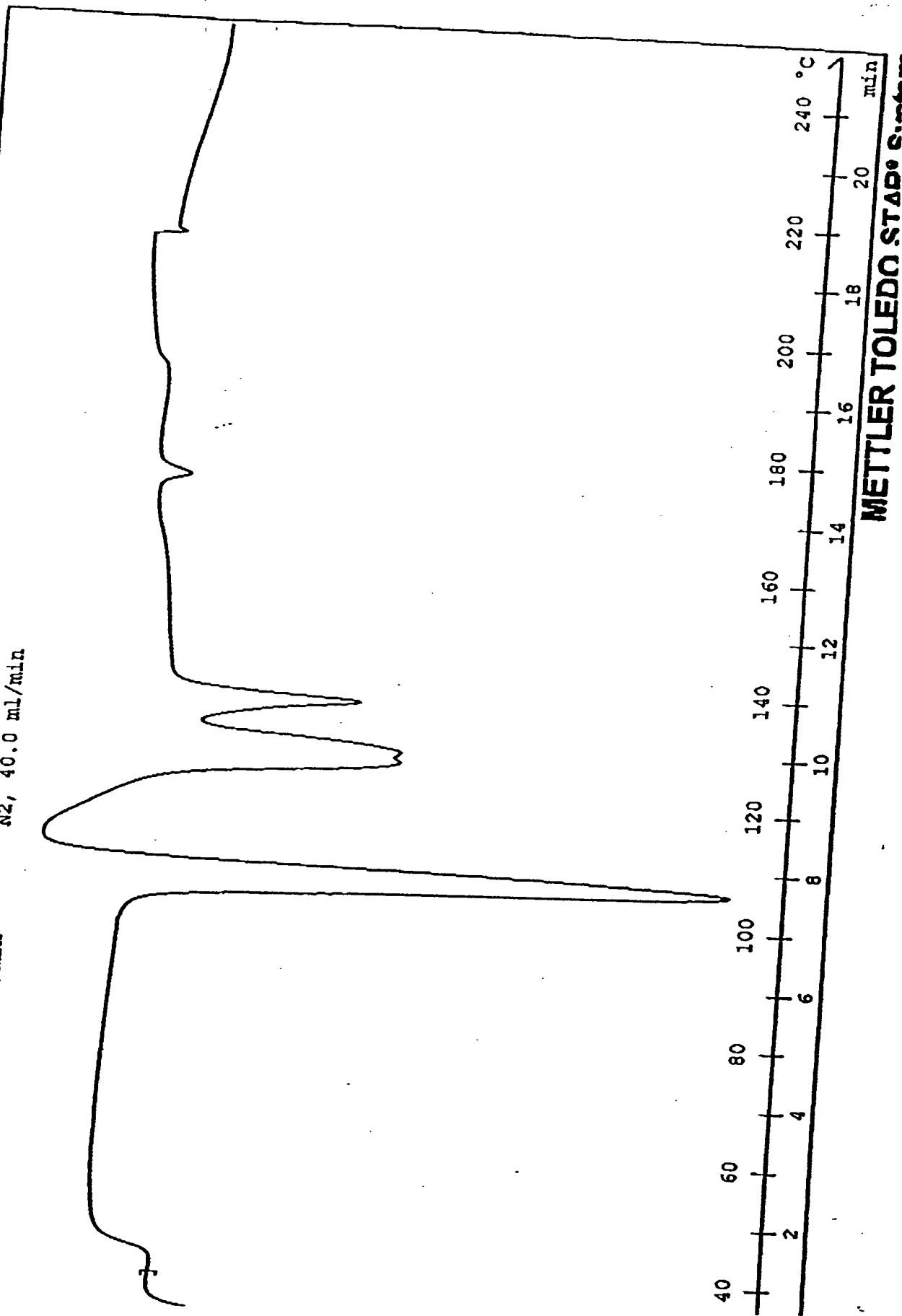


FIGURE 4.8  
Form P

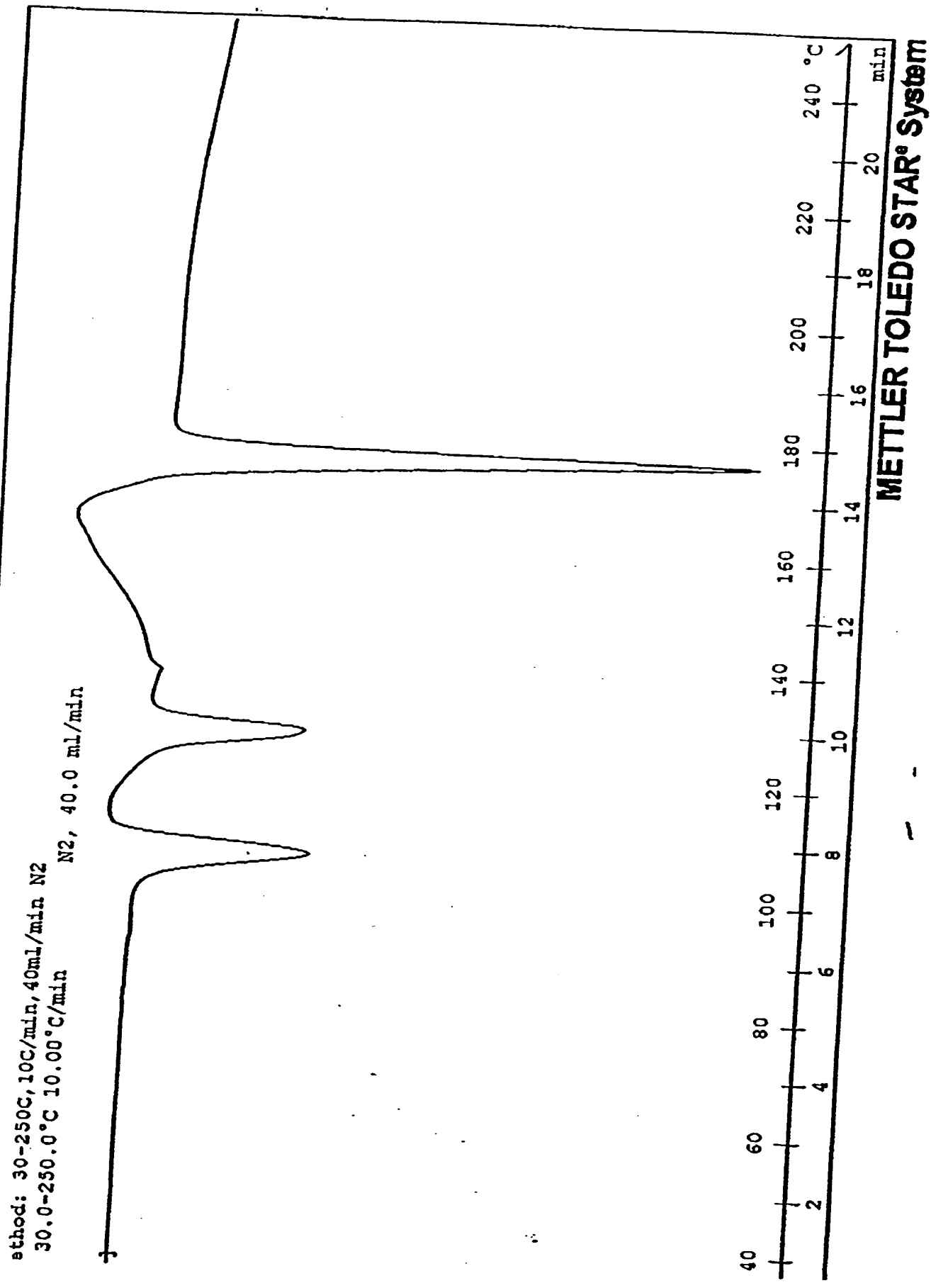




FIGURE 47 49  
Form Q

Method: 30-250°C, 10°C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

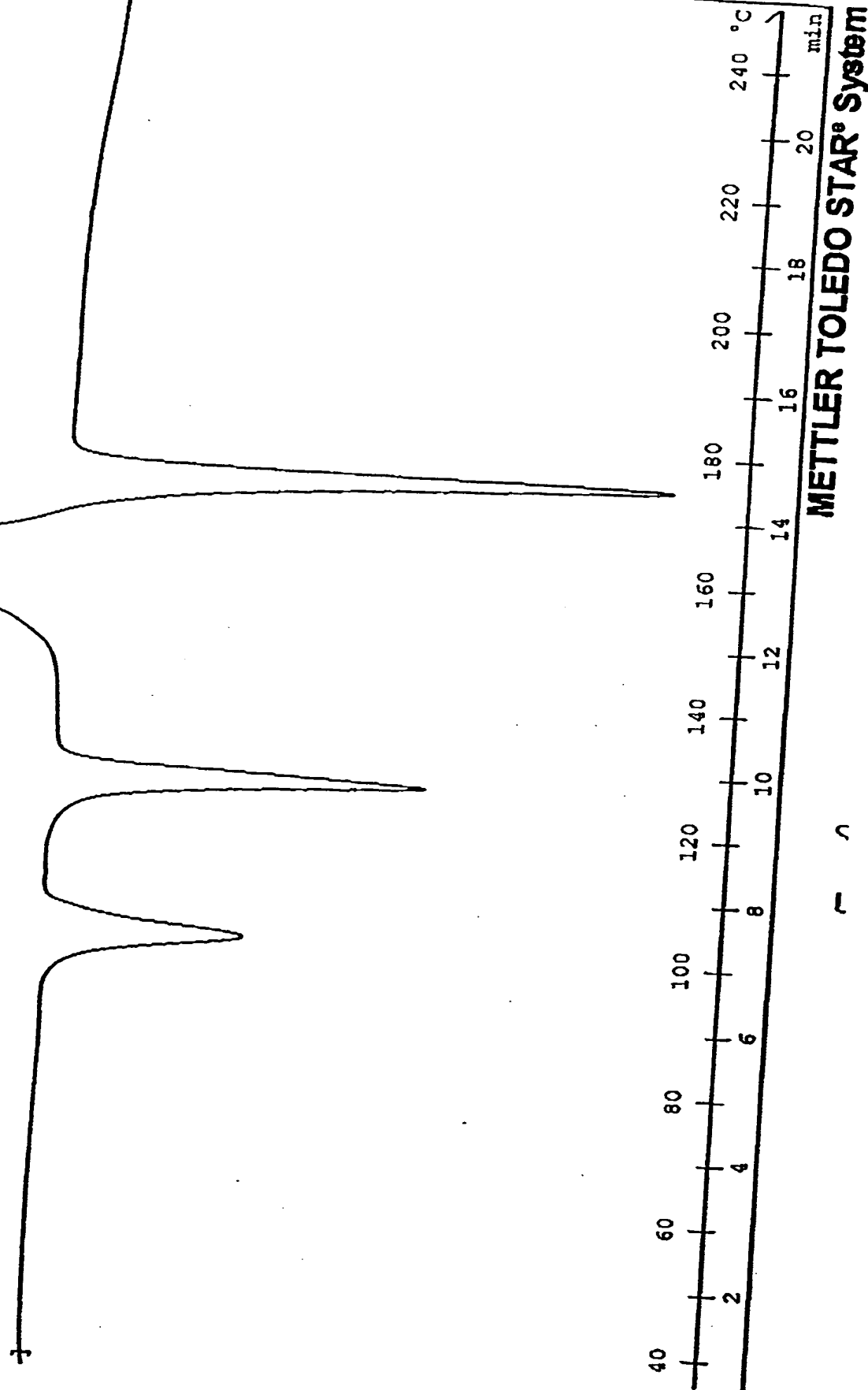
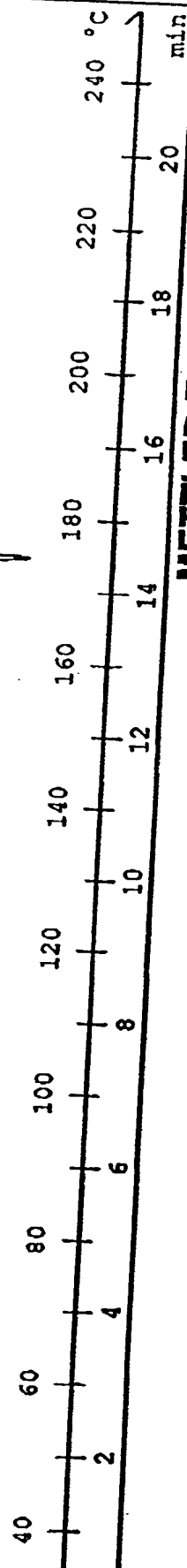


FIGURE 48 50  
Form T

Method: 30-250°C, 10°C/min, 40ml/min N<sub>2</sub>  
30.0-250.0°C 10.00°C/min  
N<sub>2</sub>, 40.0 ml/min

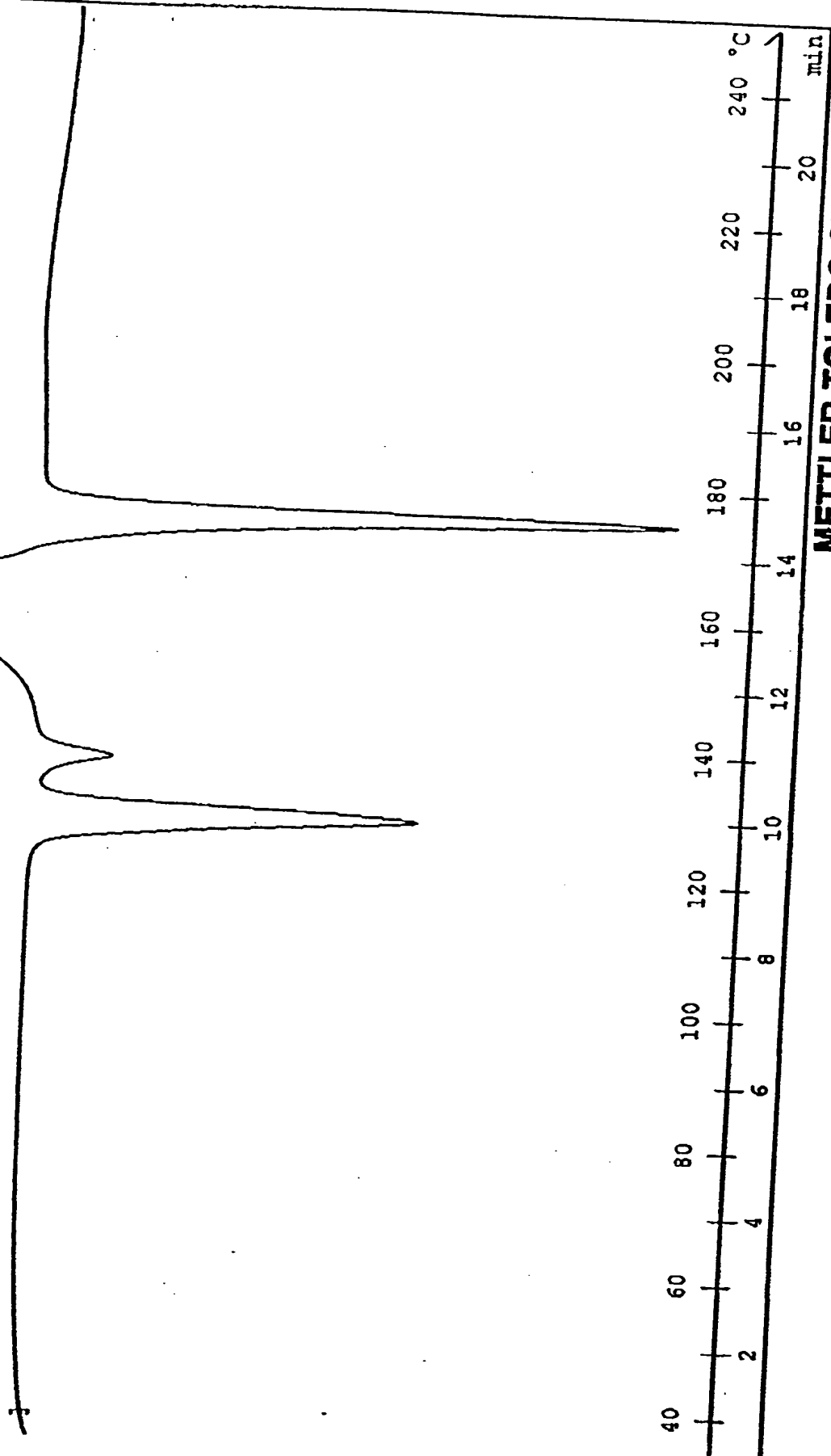


METTLER TOLEDO STAR® System

FIGURE 49. 51

Form 1A

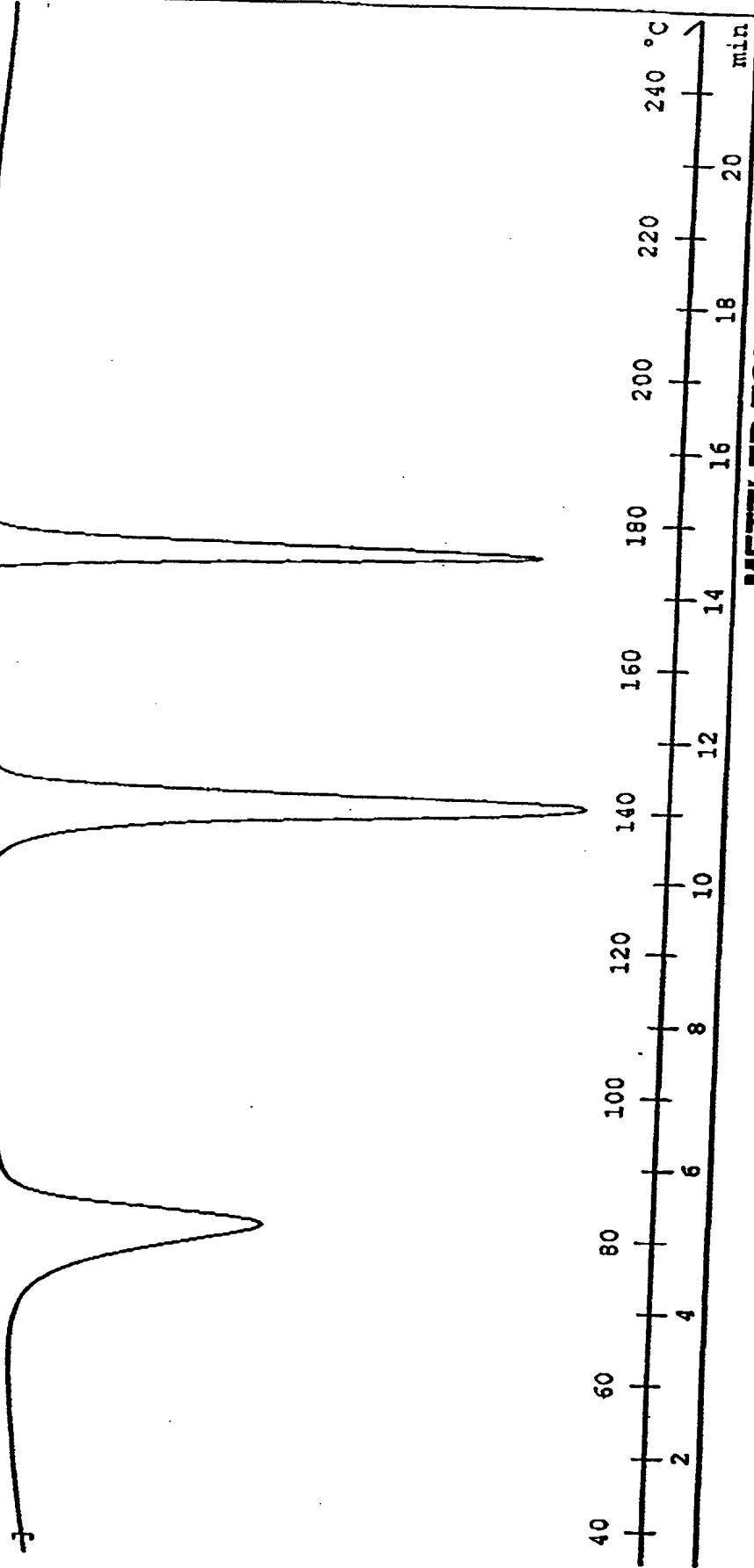
Method: 30-250C, 10C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE 5052  
Form V

Method: 30-250°C, 10°C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

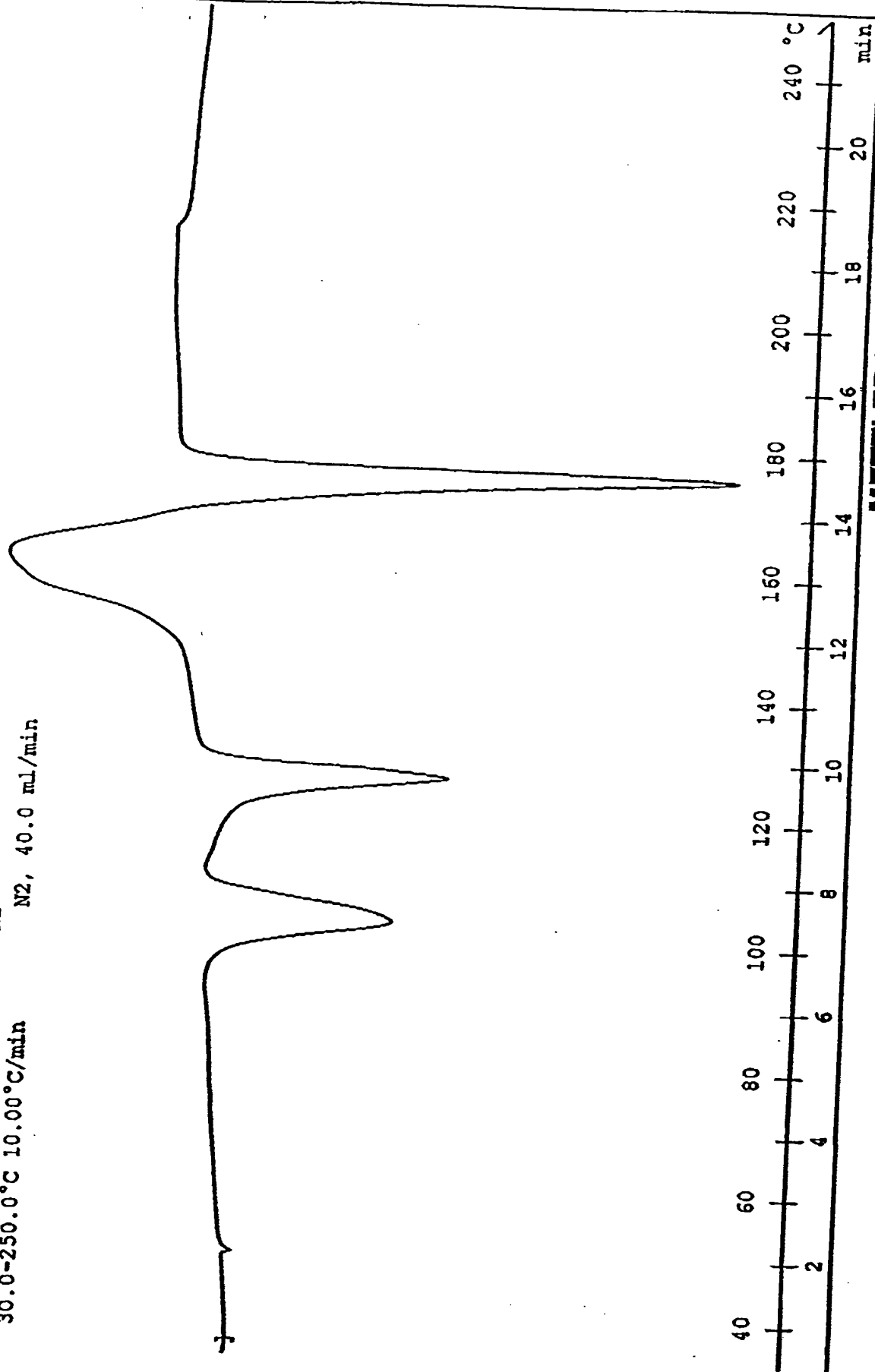
FIGURE 52-53

Fern Y (chloroform solvent)

Method: 30-250°C, 10°C/min, 40ml/min N2

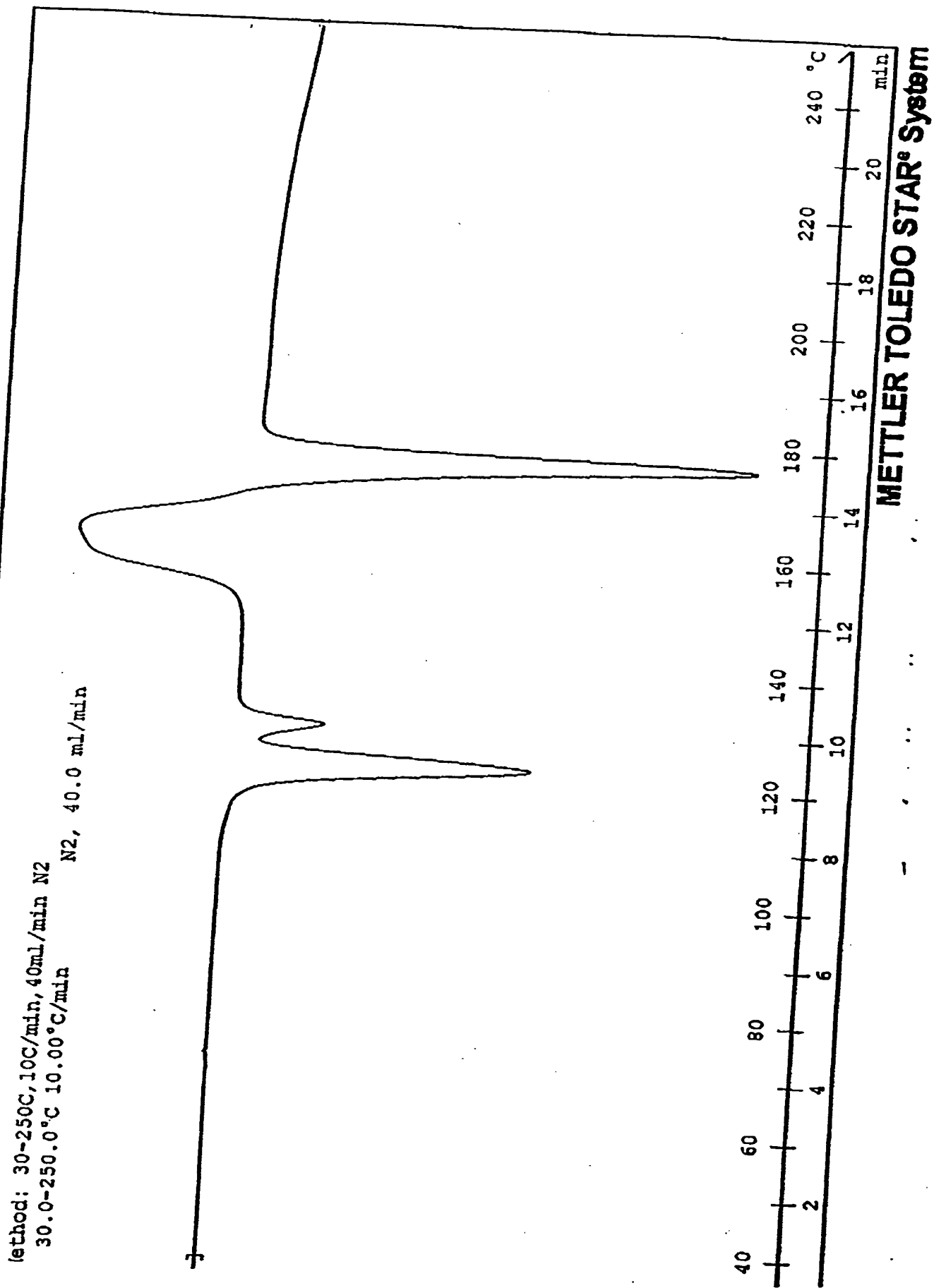
30.0-250.0°C 10.00°C/min

N2, 40.0 ml/min



METTLER TOLEDO STAR® System

Figure 5.4  
Y (dichloromethane solvent)



55  
Figure 27 - Nataglinde Form Z

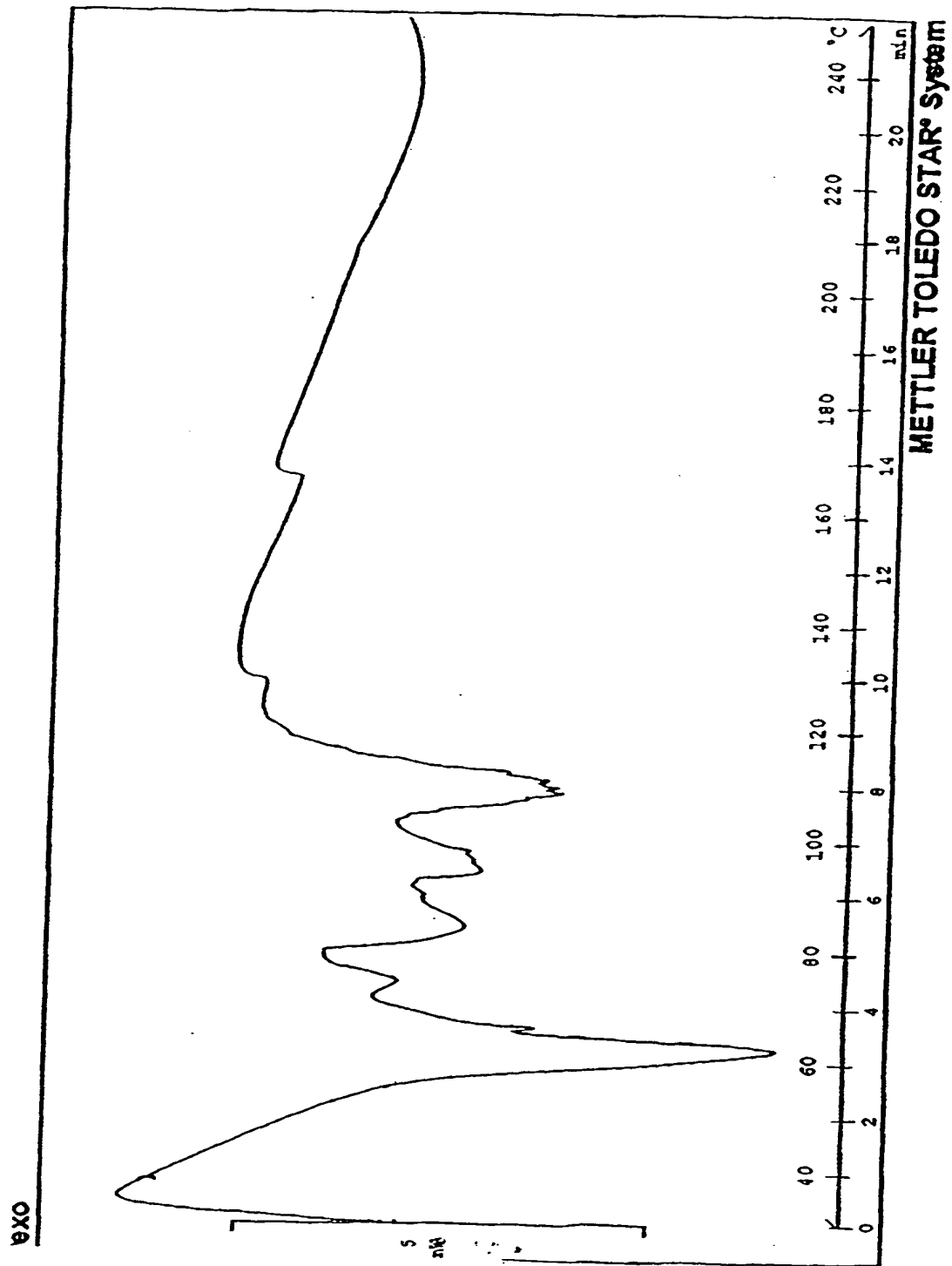
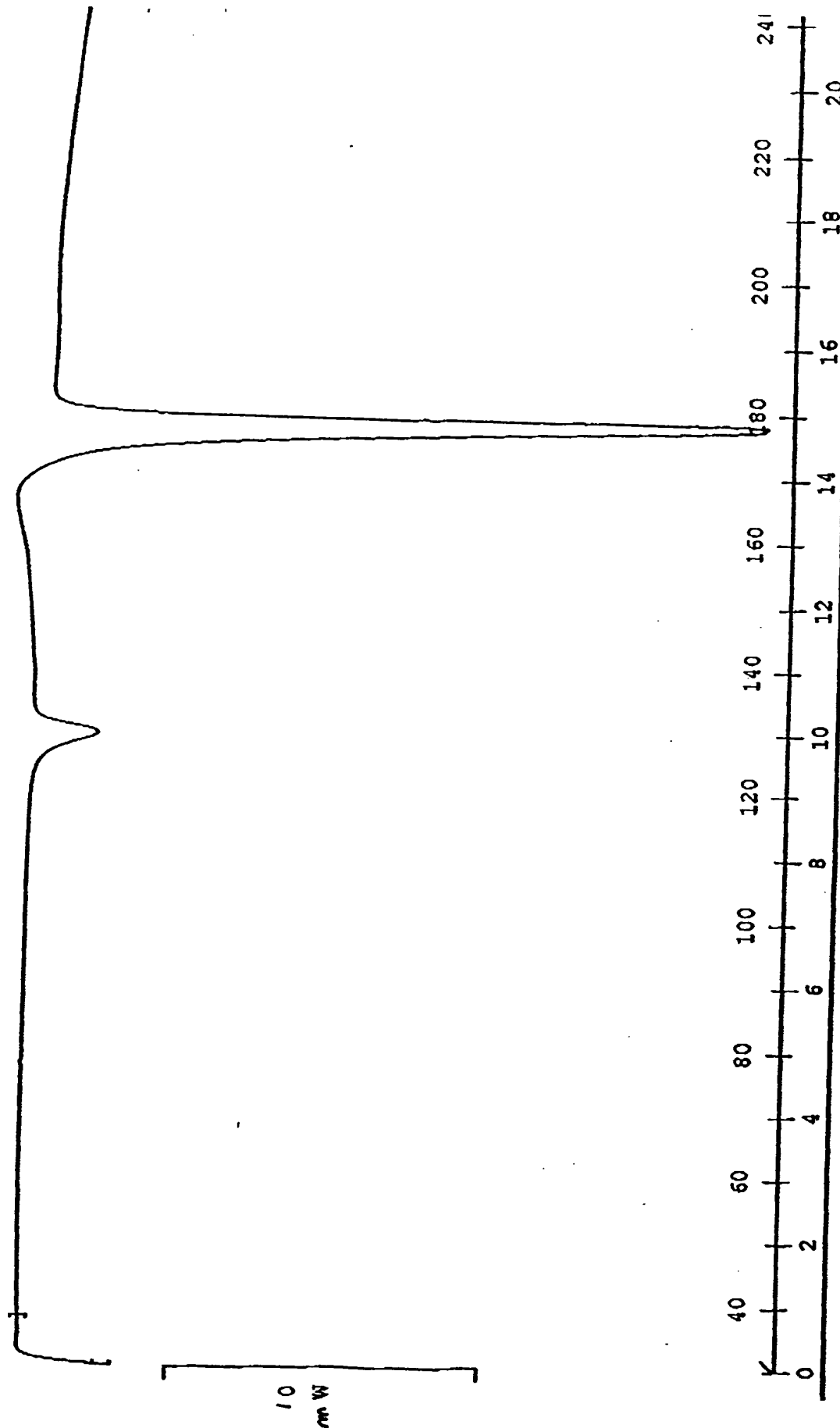


FIGURE 51-56  
Form  $\alpha$

IXO

Method: 30-250°C, 10°C/min, 40ml/min N<sub>2</sub>  
30.0-250.0°C 10.00°C/min N<sub>2</sub>, 40.0 ml/min

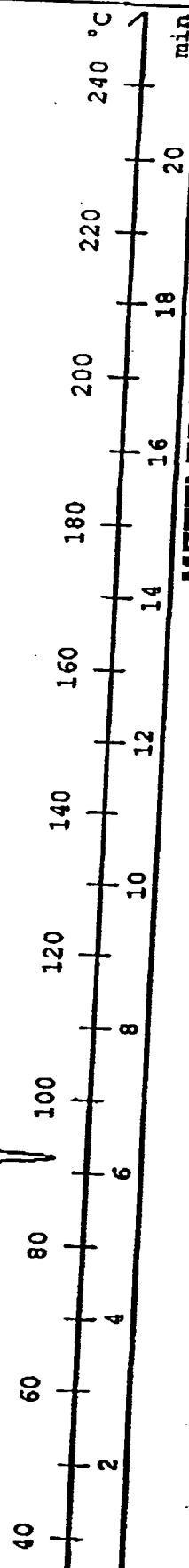


METTLER TOLEDO STAR<sup>®</sup> SW



FLUKE 57  
Form Beta

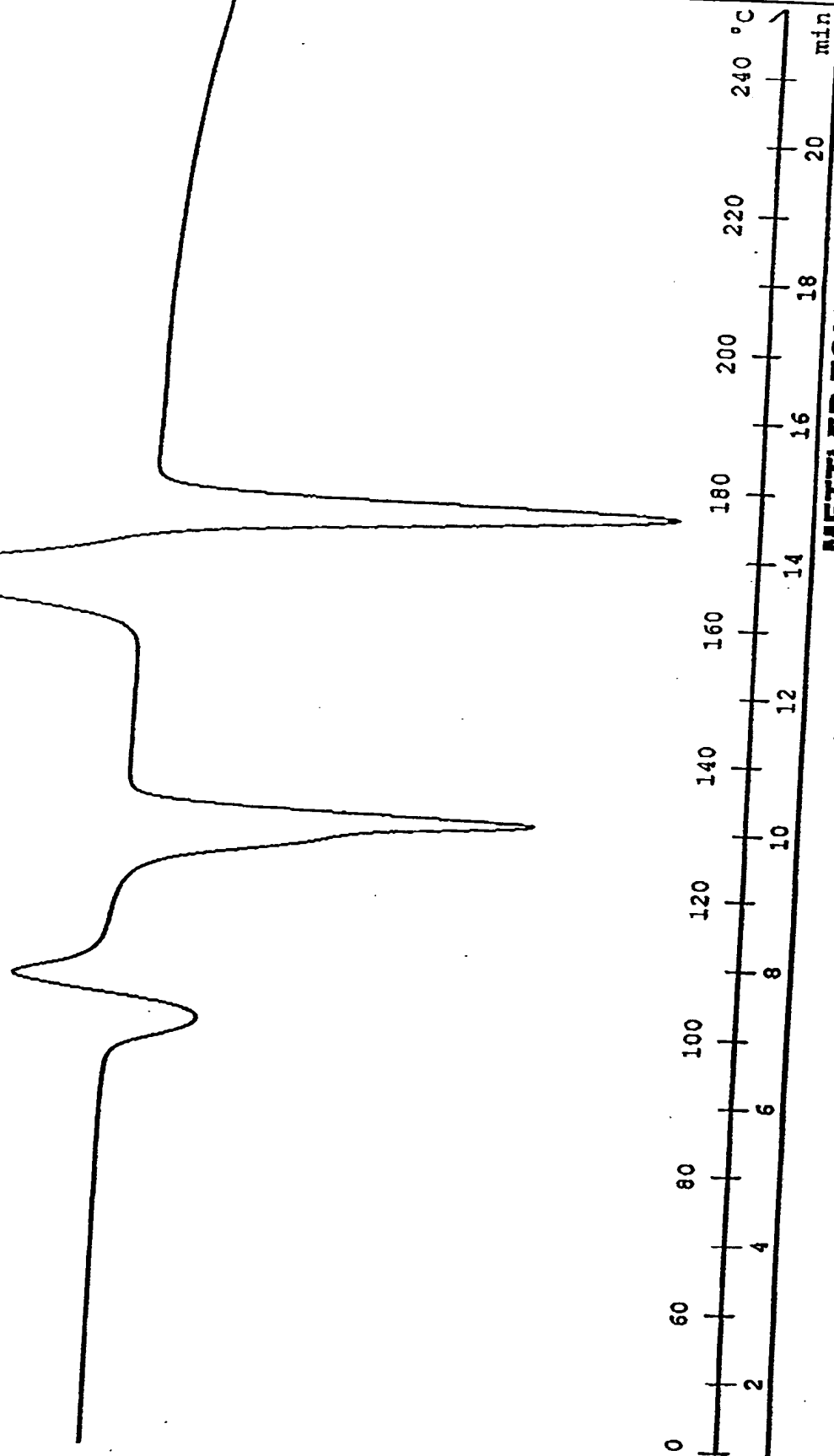
Method: 30-250°C, 10°C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min  
N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE 55-58  
Form Delta

Method: 30-250C, 10C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



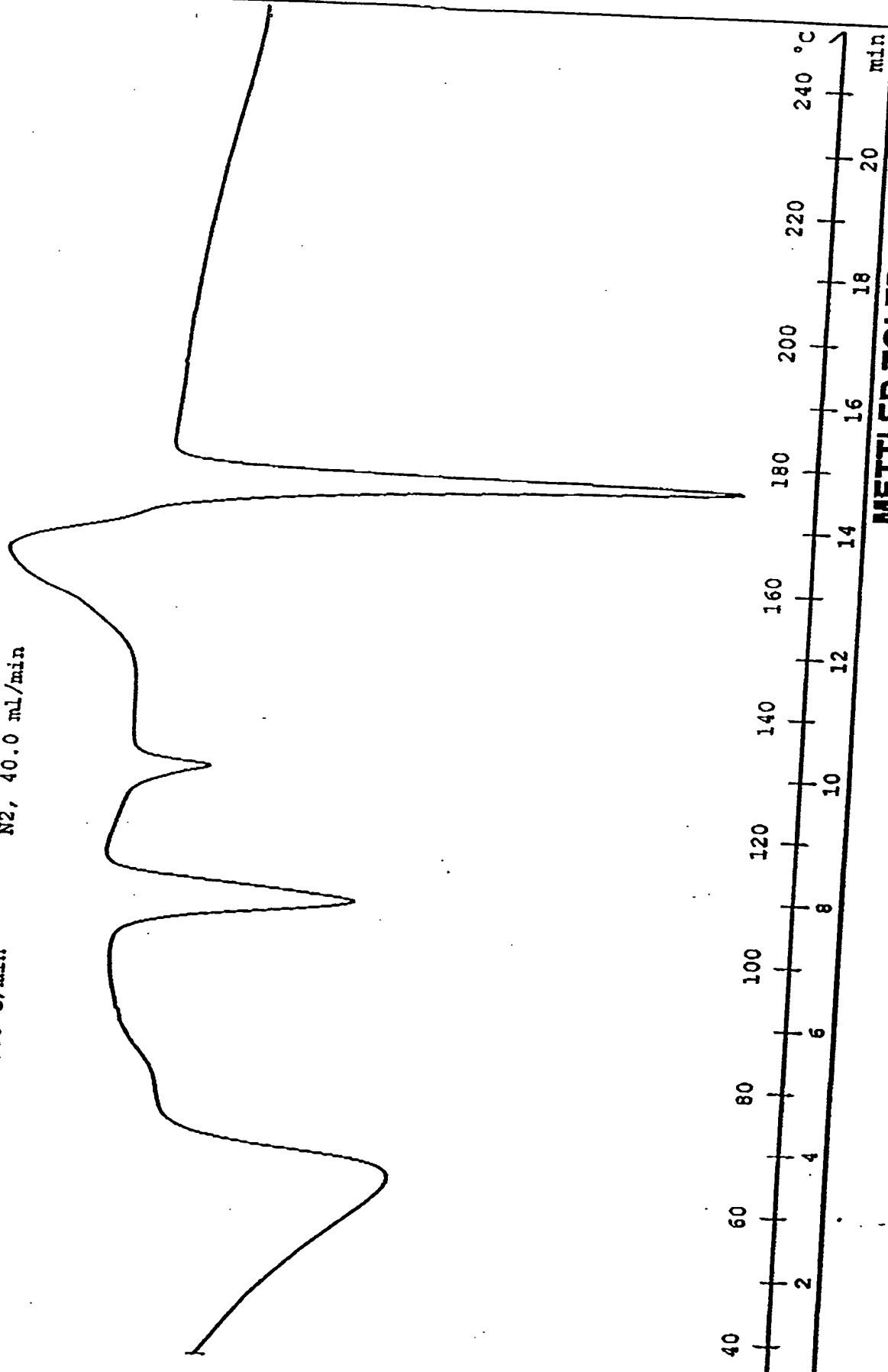
METTLE TOLEDO STAR° System

- Delta

Form Epsilon <sup>59</sup>

FIGURE 56

Method: 30-250°C, 10°C/min, 40 ml/min N<sub>2</sub>  
30.0-250.0°C 10.00°C/min  
N<sub>2</sub>, 40.0 ml/min

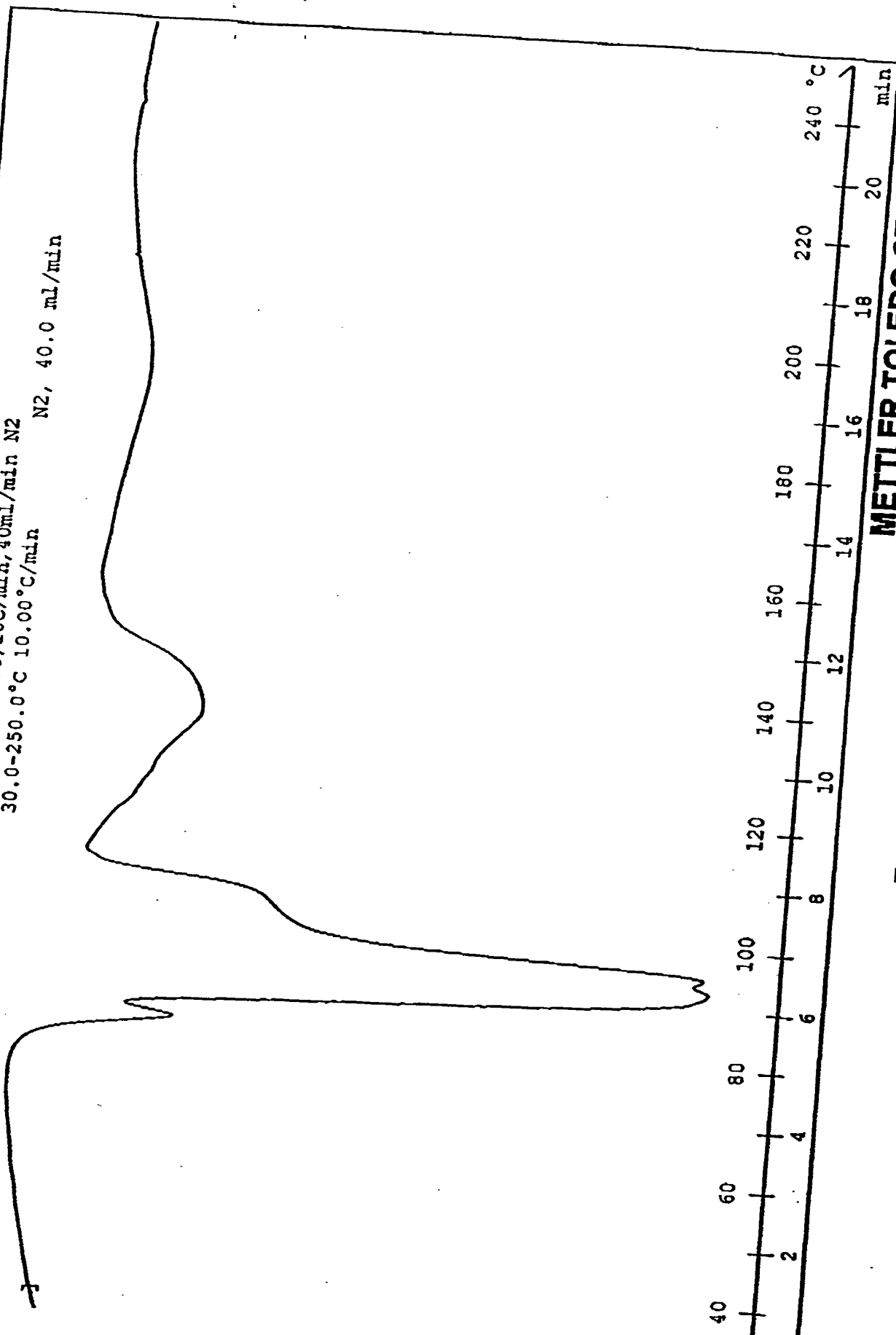


METTLER TOLEDO STAR® System

FIGURE 57  
60

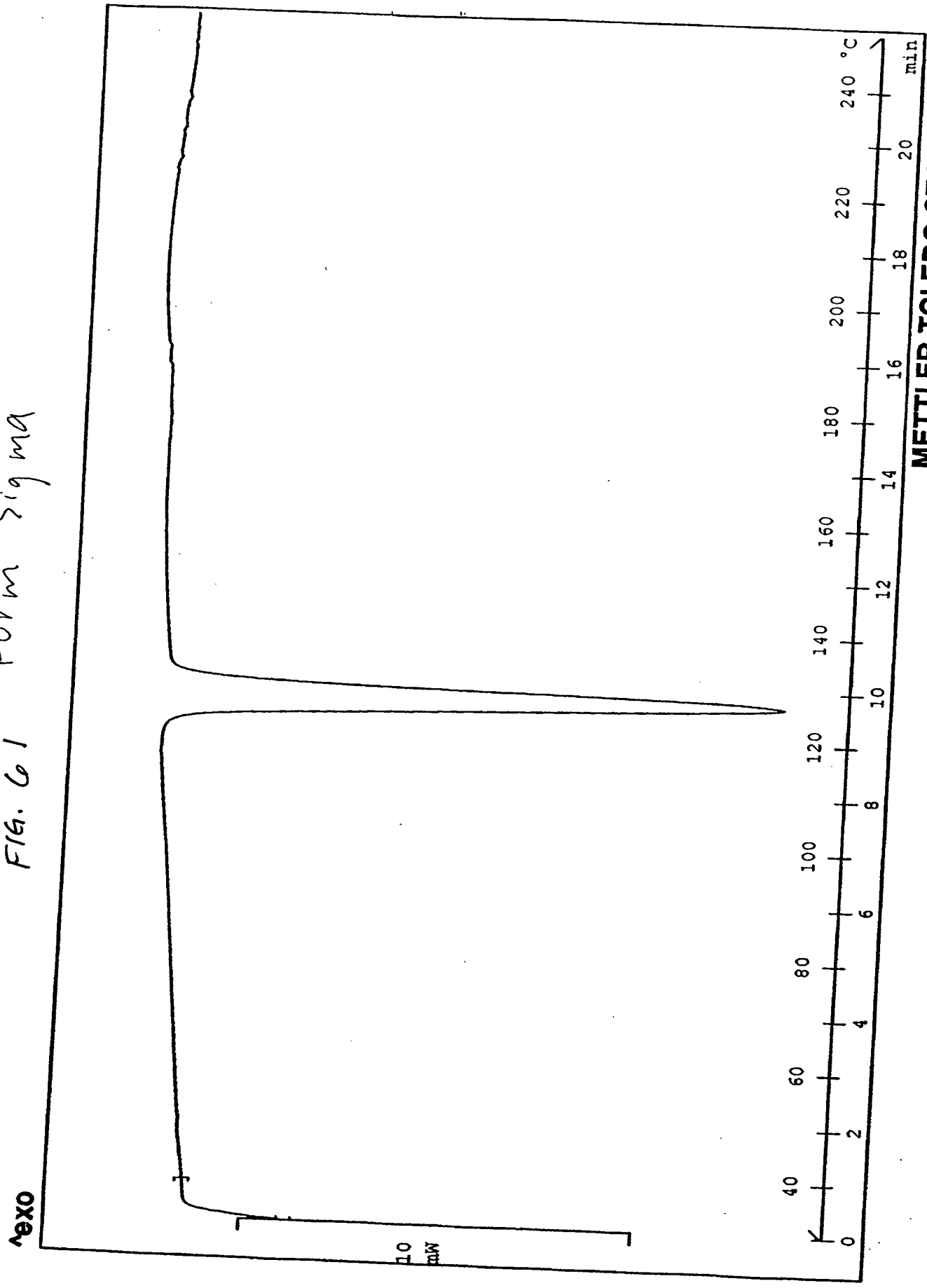
Form ~~P~~ Gamma

Method: 30-250C, 10C/min, 40ml/min N2  
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

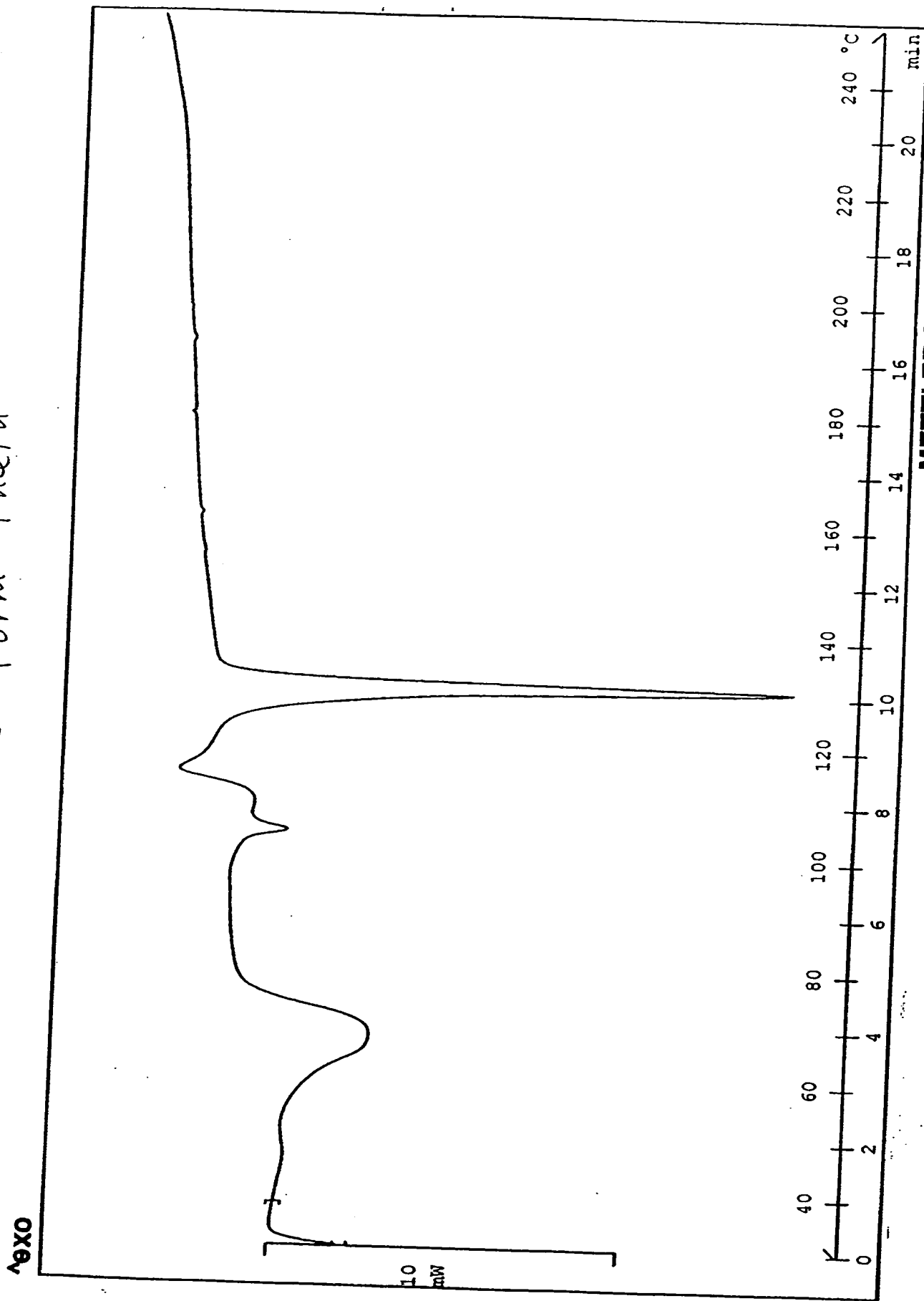
FIG. 61 Form Sigma



METTLER TOLEDO STAR® System

Form  $\sigma$  (Q)

FIGURE 62 Form Theta



METTLER TOLEDO STAR® System

Form Θ

Figure 63

Omega wet

Step.: 0.050° Cnt Time: 0.600 Sec.  
Range: 2.00 - 30.00 (Deg) Cont. Scan Rate : 5.00 Deg/min.

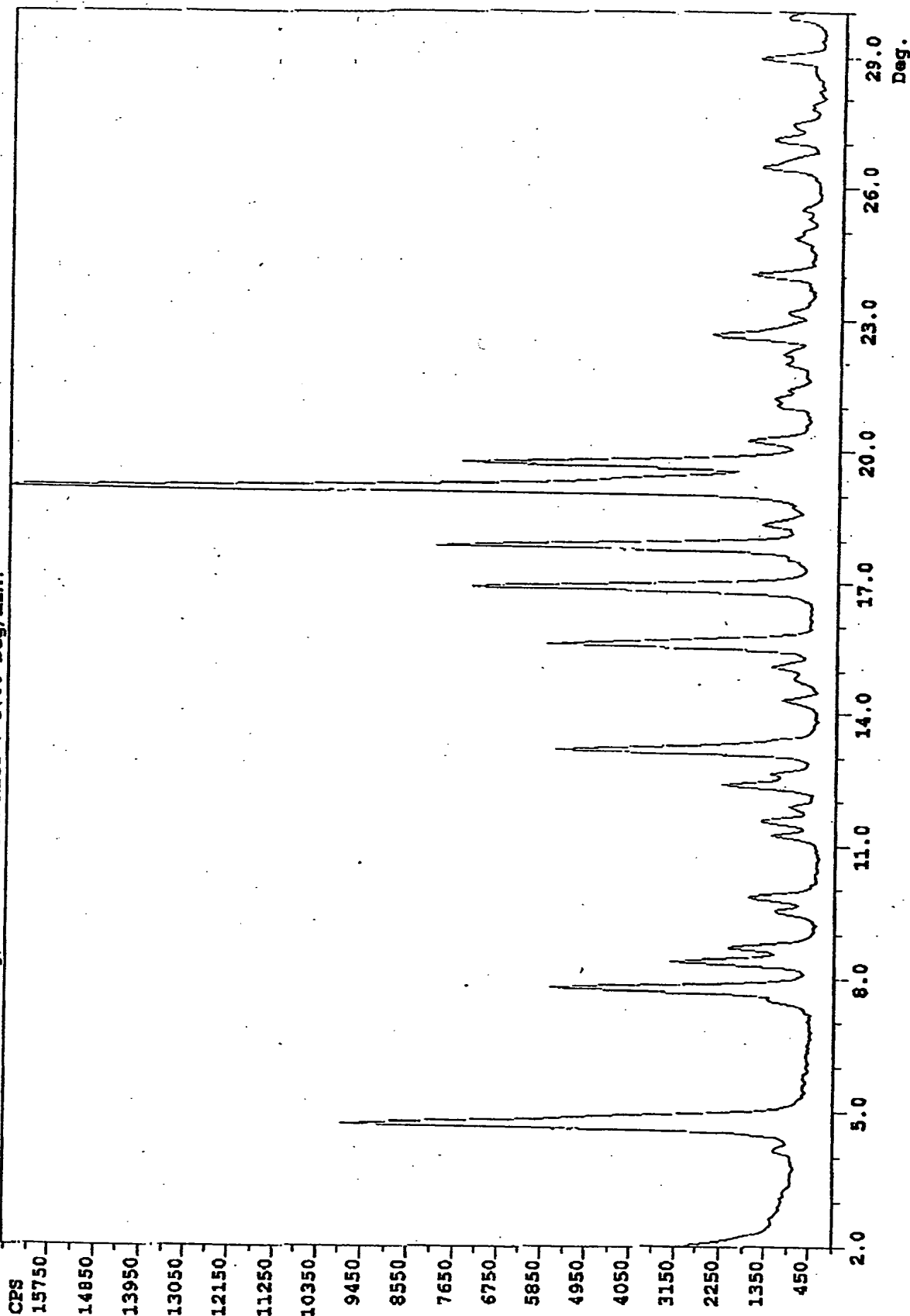


Figure 64

Comparison between the impurity profile of Nateglinide crystallized in IPA-H<sub>2</sub>O and Nateglinide crystallized in Methanol-H<sub>2</sub>O

| Sample No | Solvent                   | Impurity profile by RRT [% w/w] |        |        |        |                 |                 |                        |
|-----------|---------------------------|---------------------------------|--------|--------|--------|-----------------|-----------------|------------------------|
|           |                           | D-PA<br>(0.23)                  | (0.25) | (0.46) | (0.80) | Ipcha<br>(0.89) | Dimer<br>(1.38) | Methyl Ester<br>(1.51) |
| RL-2155/1 | Methanol-H <sub>2</sub> O | <0.01                           |        | 0.02   | <0.01  | 0.03            | 0.02            | 2.91                   |
| RL-2163/4 | IPA-H <sub>2</sub> O      | <0.01                           | 0.04   |        | 0.02   | 0.02            | 0.01            | 0.04                   |
|           |                           |                                 |        |        |        |                 |                 | 0.03                   |
|           |                           |                                 |        |        |        |                 |                 | 0.02                   |
|           |                           |                                 |        |        |        |                 |                 | 0.02                   |

Note: D-PA means D-Phenyl Alanine

Ipcha means Iso propyl cyclohexyl carboxylic acid

Both are the starting materials of the product

(-)-N-[(trans-4-isopropyl cyclohexane)carbonyl]-D-phenylalanine



**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☒ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**